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L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
2002:964996 Document No. 138:33697 Endocrine gland-derived vascular endothelial growth factor nucleic acids and polypeptides and their biological activities and use in drug screening and therapies. Ferrara, Napoleone; Watanabe, Colin; Wood, William I.; Shek, Theresa (USA). U.S. Pat. Appl. Publ. US 2002192634 A1 20021219, 105 pp., Cont.-in-part of U.S. Ser. No. 886,242. (English). CODEN: USXXCO. APPLICATION: US 2001-27603 20011219. PRIORITY: US 1998-PV96146 19980811; WO 1999-US12252 19990602; US 1999-PV145698 19990726; US 1999-380137 19990825; WO 2000-US219 20000105; WO 2000-US4914 20000224; WO 2000-US8439 20000330; US 2000-PV213637 20000623; US 2000-PV230978 20000907; US 2000-709238 20001108; WO 2000-US32678 20001201; US 2001-886242 20010620.

AB The present invention is based on the identification and characterization of a novel, tissue-restricted, growth and differentiation factor that acts selectively on one endothelial cell type. This factor, referred to as endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**), induces proliferation, migration, and fenestrations in capillary endothelial cells derived from endocrine glands, but has no

effect on a variety of other endothelial and non-endothelial cell types tested. **EG-VEGF** also induces phosphorylation of kinases involved in cell proliferation or survival, including ERK1, ERK2, Akt, and eNOS. **EG-VEGF** nucleic acids and polypeptides can be used in a no. of assays and in diagnosis and treatment of conditions assocd. with hormone-producing tissue. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, **antibodies** which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Also provided herein are methods of screening for modulators of **EG-VEGF**. Furthermore, methods and related methods of treatment are described herein which pertain to regulating cellular proliferation and chemotaxis.

=> d l3 cbib abs 1-55

L3 ANSWER 1 OF 55 CAPLUS COPYRIGHT 2003 ACS on STN
2003:418757 Document No. 139:163373 Preparation, characterization and function assay of monoclonal **antibodies** to human CD38. Wen, Xinyu; Shu, Cuiling; Yu, Ming; Li, Yan; Qi, Zhongtian; Shen, Beifen (Institute of Basic Medical Sciences, Academy of Military Medical Sciences, Beijing, 100850, Peop. Rep. China). Mianyixue Zazhi, 19(1), 69-71, 74 (Chinese) 2003. CODEN: MIZAED. ISSN: 1000-8861. Publisher: Mianyixue Zazhi Bianjibu.

AB The McAb to human CD38 was prepd. for studying the biol. function of this mol. Daudi cell line which highly expresses CD38 mol. was used as antigen to immunize Balb/c mice. The spleen cells of the immunized mice were used to prep. the McAb by hybridoma techniques. Hybridoma cells was selected by indirect immunofluorescence expts., immunopptn. and flow cytometry (FCM) anal. and western blot anal. with the recombinant CD38 protein were used to identify specificity of the prepd. McAb. CDC expt. and cell proliferation inhibition expt. were examd. by MTT. A monoclonal **antibody** against CD38 was obtained by hybridoma techniques and named as **1C6**. The results of immunopptn. showed that the **antibody** could recognize 45 000 u mols. on the surface of Daudi cell. FCM anal. indicated that **1C6** accorded with anti-CD38 McAb in specific reaction with cell lines. Western blot anal. revealed that **1C6** could recognize the recombinant CD38 protein. Functional assay revealed that **1C6** could markedly kill target cells by CDC (complement dependant cytotoxicity). A hybridoma cell line **1C6** secreting anti-CD38 McAb stably was established and characterized.

L3 ANSWER 2 OF 55 MEDLINE on STN DUPLICATE 1
2002696340 Document Number: 22345083. PubMed ID: 12457033. Clinical significance of angiogenic factor expression at the deepest invasive site of advanced colorectal carcinoma. Kaio Eijiro; Tanaka Shinji; Kitadai Yasuhiko; Sumii Masaharu; Yoshihara Masaharu; Haruma Ken; Chayama Kazuaki. (The First Department of Internal Medicine, Hiroshima University School of Medicine, Hiroshima, Japan.) ONCOLOGY, (2003) 64 (1) 61-73. Journal code: 0135054. ISSN: 0030-2414. Pub. country: Switzerland. Language: English.

AB Tumor angiogenesis is a complicated process for which the mechanisms remain unclear. The aim of this study was to elucidate the clinical significance of several angiogenic factor expression as a predictor of the invasive/metastatic potential and of the prognosis of advanced colorectal carcinoma (CRC) in relation to their intratumoral histologic heterogeneity. One hundred fifty two patients who had undergone surgical resection for advanced CRC entered this study. PD-ECGF, VEGF, and VEGF-C were examined immunohistochemically with **antibodies 1C6** -203, A-20, and C-20, respectively. Tumor microvessel density (MVD) was determined immunohistochemically with anti-CD34 **antibody**. Expression of PD-ECGF, of VEGF, and of VEGF-C at the deepest invasive site

were detected in 77 (50.7%), 62 (30.8%), and 71 (46.7%) of the 152 lesions, respectively. PD-ECGF, VEGF, and VEGF-C expression at the deepest invasive site in lesions with liver metastasis (77, 67, and 70%) was significantly higher than that in those without liver metastasis (44, 34, and 41%). In cases with curative surgery, patients with PD-ECGF, VEGF, and VEGF-C expression at the deepest invasive site had a significantly poorer prognosis than those without PD-ECGF, VEGF, and VEGF-C expression at the deepest invasive site. PD-ECGF, VEGF, and VEGF-C expression at the deepest invasive site correlated significantly with MVD. Multivariate analysis with logistic regression for 5-year survival in patients with curative surgery showed that lymph node metastasis and VEGF expression were significant risk factors. Expression of PD-ECGF, VEGF, and VEGF-C was correlated significantly with metastatic potential and prognosis in relation to MVD. Of the several angiogenic factors, VEGF expression at the deepest invasive site of tumor was the most statistically significant indicator of prognosis in advanced CRC.

L3 ANSWER 3 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
2003:376933 Document No.: PREV200300376933. A monoclonal **antibody** directed against SCR1-2 of complement control protein, CD55 enhances C3 deposition and tumour cell lysis. Bradley, R. G. [Reprint Author]; Morgan, J. [Reprint Author]; Spendlove, I. [Reprint Author]; Durrant, L. G. [Reprint Author]. Academic Unit of Clinical Oncology, CRUK, Nottingham University, Nottingham City Hospital, Nottingham, UK. British Journal of Cancer, (July 2003) Vol. 88, No. Supplement 1, pp. S39. print.
Meeting Info.: British Cancer Research Meeting 2003. Bournemouth, UK. July 02-05, 2003.
ISSN: 0007-0920 (ISSN print). Language: English.

L3 ANSWER 4 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
2003:343871 Document No.: PREV200300343871. Detection of antigenic determinants at the N-terminal region of the VP35 protein of the Ebola virus by using the short recombinant fragments of the mentioned protein. Rudzevich, T. N.; Ternovoy, V. A.; Kazachinskaya, E. I.; Razumov, T. A.; Chepurnov, A. A.; Netesov, S. V.. Molekulyarnaya Genetika Mikrobiologiya i Virusologiya, (2003) No. 2, pp. 38-41. print.
CODEN: MGMVDU. ISSN: 0208-0613. Language: Russian.
AB cDNA of fragments of gene VP35 of the Ebola virus (EV) were expressed in vector pQE30 for the purpose of isolation of recombinant fragments of protein VP35. Five short affinity-purified fragments of the EV VP35 protein were analyzed, by using the methods of IEA and immunoblotting, with polyclonal antiviral sera (PAS) against EV and with hybrid monoclonal **antibodies** (Mabs) **1C6** and 6F7 specific to EV VP35 protein. All fragments of protein VP35 with an intact N-terminal region and removed C-terminal region were found to interact effectively with PAS and with Mabs **1C6** and 6F7. Rec86N, the smallest of the above fragments, comprised the initial 86 amino acid residues of the VP35 N-terminal region. A removal of 36 amino acid residues from the N-terminal region of Rec310N, the largest recombinant fragment, resulted in a loss of interaction with Mabs **1C6** and 6F7, while the interaction with polyclonal **antibodies** remained intact. The obtained results show that the initial 86 amino acid residues of the N-terminal region of EV VP35 are of the key importance in forming the antigenic structure of VP35 and that they contain multiple B-cell epitopes. Finally, the initial 36 amino acids of VP35 predetermine the shaping-up of two antigenic determinants for Mabs **1C6** and 6F7.

L3 ANSWER 5 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
2003:580861 Document No.: PREV200300571440. PROGNOSTIC EFFECT OF THYMIDINE PHOSPHORYLASE, DIHYDROPYRIMIDINE DEHYDROGENASE, AND P-GLYCOPROTEIN IN COLORECTAL CANCER: IMMUNOHISTOCHEMISTRY WITH NEW MONOCLONAL **ANTIBODIES** . Tokunaga, Yukihiko [Reprint Author]; Saito, Toru

[Reprint Author]. Osaka, Japan. Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. M1523. e-file. Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract. Language: English.

AB Aims: Thymidine phosphorylase (TP) is an essential enzyme for activation of 5-fluorouracil (5FU) and its derivatives. Dihydropyrimidine dehydrogenase (DPD) is a rate-limiting enzyme for degradation of 5FU. P-Glycoprotein(PG), a product of the multidrug resistance gene, may be one of the mechanism of drug resistance. In colorectal cancer (CRC), several studies evaluated the relationship between TP, DPD, PG, and clinicopathologic features. However, the results may not be definitive since monoclonal **antibody** sensitive for human TP and DPD has not been established. Now, new monoclonal **antibodies** for human TP (**1C6**-203) and human DPD (2H9-1b) are available. Patients and Methods: The study included 100 patients whose CRCs were classified into stage II to IV, and resected surgically between 1990 and 2002. TP, DPD, and PG expression were evaluated using immunohistochemistry with new **antibodies**. Relationships between these expression and clinicopathological features were eveluated. Survival curves, calculated using Kaplan-Meier method, were evaluated with log-rank test. Cox proportional hazards model was also used. Results: TP and DPD expression showed positive correlations with advances in lymphatic invasion (p=0.04 and 0.06 respectively), venous invasion (p=0.03 and 0.03), and cancer stage (p=0.003 and 0.03). PG was correlated with histological differentiation (p=0.02). The patients survival rates were higher in those TP(-) than in those TP(+) (p=0.02), and higher in those DPD(-) than in those DPD(+) (p=0.02). Thus, the survival rates declined according to DPD and TP status as follows; DPD(-) TP(+) >= DPD(-) TP(-) > DPD(+) TP(-) > DPD(+) TP(+). The estimated hazard ratio for patients death with TP and DPD expression were 4.6 and 4.8 (p=0.01 and 0.03) respectively. However, PG was not a prognostic factor. Conclusions: Using new sensitive monoclonal **antibodies** to TP and DPD, the present results indicated that TP and DPD expression are associated with CRC progression and invasion, and closely related with poor prognosis in postoperative CRC patients. Moreover, TP and DPD expression are significant prognostic factors..

L3 ANSWER 6 OF 55 CAPLUS COPYRIGHT 2003 ACS on STN

2002:964996 Document No. 138:33697 Endocrine gland-derived vascular endothelial growth factor nucleic acids and polypeptides and their biological activities and use in drug screening and therapies. Ferrara, Napoleone; Watanabe, Colin; Wood, William I.; Shek, Theresa (USA). U.S. Pat. Appl. Publ. US 2002192634 A1 20021219, 105 pp., Cont.-in-part of U.S. Ser. No. 886,242. (English). CODEN: USXXCO. APPLICATION: US 2001-27603 20011219. PRIORITY: US 1998-PV96146 19980811; WO 1999-US12252 19990602; US 1999-PV145698 19990726; US 1999-380137 19990825; WO 2000-US219 20000105; WO 2000-US4914 20000224; WO 2000-US8439 20000330; US 2000-PV213637 20000623; US 2000-PV230978 20000907; US 2000-709238 20001108; WO 2000-US32678 20001201; US 2001-886242 20010620.

AB The present invention is based on the identification and characterization of a novel, tissue-restricted, growth and differentiation factor that acts selectively on one endothelial cell type. This factor, referred to as endocrine gland-derived vascular endothelial growth factor (EG-VEGF), induces proliferation, migration, and fenestrations in capillary endothelial cells derived from endocrine glands, but has no effect on a variety of other endothelial and non-endothelial cell types tested. EG-VEGF also induces phosphorylation of kinases involved in cell proliferation or survival, including ERK1, ERK2, Akt, and eNOS. EG-VEGF nucleic acids and polypeptides can be used in a no. of assays and in diagnosis and treatment of conditions assocd. with hormone-producing tissue. Also provided herein are vectors and host cells comprising those

nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, **antibodies** which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Also provided herein are methods of screening for modulators of EG-VEGF. Furthermore, methods and related methods of treatment are described herein which pertain to regulating cellular proliferation and chemotaxis.

L3 ANSWER 7 OF 55 MEDLINE on STN DUPLICATE 3
2002279349 Document Number: 22014263. PubMed ID: 12019408. Prognostic value of thymidine phosphorylase/platelet-derived endothelial cell growth factor in advanced colorectal cancer after surgery: evaluation with a new monoclonal **antibody**. Tokunaga Yukihiko; Hosogi Hisahiro; Hoppou Toshitaka; Nakagami Mikio; Tokuka Atsuo; Ohsumi Kiyoshi. (Department of Surgery, Maizuru Municipal Hospital, Kyoto, Japan.) SURGERY, (2002 May) 131 (5) 541-7. Journal code: 0417347. ISSN: 0039-6060. Pub. country: United States. Language: English.

AB BACKGROUND: Thymidine phosphorylase (TP) is an essential enzyme for activation of 5-fluorouracil and its derivatives and identical to platelet-derived endothelial cell growth factor. In colorectal cancer (CRC), previous studies evaluating the relationship between TP expression and clinicopathologic features have yielded inconsistent results. These studies used monoclonal **antibody** 654-1, which stained CRC cells weakly. Now, a new monoclonal **antibody**, **1C6**-203, more sensitive than 654-1, is available. METHODS: This study included 80 patients whose CRCs were classified into stages II to IV and completely resected surgically in our institute. TP expression in CRC was evaluated by using immunohistochemical staining with **1C6**-203. Relationships between TP expression and clinicopathologic variables that might have affected the patients' prognosis were evaluated. Survival curves were calculated with the Kaplan-Meier method, and differences were evaluated with log-rank test. Cox proportional hazards model was used in the univariate and multivariate survival analyses. RESULTS: TP expression showed a positive correlation with advances in histologic differentiation (P =.025), lymph node metastasis (P =.083), lymphatic invasion (P =.049), venous invasion (P =.042), and cancer stage (P =.002). The patients' survival rates after surgery were higher (P =.0041) in those with negative TP than in those with positive TP. The overall estimated hazard ratio for death in patients with TP expression was 6.24 according to univariate analysis (P =.013). Multivariate analysis showed that TP was a significant prognostic factor adjusted for other clinicopathologic variables. CONCLUSIONS: With a new highly sensitive monoclonal **antibody** to TP, the present results indicated that TP expression is associated with CRC progression and invasion and closely correlated with poor prognosis in postoperative CRC patients. Moreover, TP expression is an independent prognostic factor in CRC patients.

L3 ANSWER 8 OF 55 MEDLINE on STN DUPLICATE 4
2002045117 Document Number: 21628920. PubMed ID: 11755674. Anti-immunoglobulin binding and activation of snapper (Pagrus auratus) leucocytes. Morrison Richard N; Hayball John D; Cook Mathew T; Nowak Barbara F. (School of Aquaculture and CRC for Aquaculture, Tasmanian Aquaculture and Fisheries Institute, University of Tasmania, Launceston, Tasmania, Australia, 7250.. rmorriso@utas.edu.au) . DEVELOPMENTAL AND COMPARATIVE IMMUNOLOGY, (2002 Apr) 26 (3) 247-55. Journal code: 7708205. ISSN: 0145-305X. Pub. country: United States. Language: English.

AB In order to perform specific immunological assays we have produced and characterised three monoclonal **antibodies** (MAbs) that bind snapper (Pagrus auratus, Bloch and Schneider) immunoglobulin (Ig). Hybridomas were produced and screened for anti-Ig production using ELISA, Western blot and flow cytometry. All three MAbs (designated 2C5, 4A2 and **1C6**) bound specifically to the heavy (H) chain of reduced Ig in Western blot. Furthermore, **1C6** was shown to bind to reduced

skin mucus Ig H chain and all three MAbs cross-reacted with the H chain of Atlantic salmon and rainbow trout Ig. In flow cytometric analyses 2C5 and 4A2 bound to B cell populations in the peripheral blood and lymphoid organs. Furthermore, cross-linked 2C5 induced an increase in intracellular protein tyrosine phosphorylation in peripheral blood lymphocytes. Phosphorylated proteins exhibited similar molecular weights to those of mammalian Igalpha and Igbeta and may represent snapper mIg accessory molecule analogues. These data exhibit the potential use of 2C5, 4A2 and **1C6** in both cellular and biochemical analyses of populations of snapper leucocytes.

L3 ANSWER 9 OF 55 MEDLINE on STN DUPLICATE 5
2002409848 Document Number: 22155122. PubMed ID: 12165145.
Characterization of four monoclonal **antibodies** to recombinant human tartrate-resistant acid phosphatase. Miyazaki Takashi; Matsunaga Toshiyuki; Miyazaki Shuichi; Hokari Shigeru; Komoda Tsugikazu. (Department of Biochemistry, Saitama Medical School, 38 Morohongo, Moroyama, Iruma-gun, Saitama 350-0495, Japan.. miyasan@ns2.saitama-med.ac.jp) . Hybrid Hybridomics, (2002 Jun) 21 (3) 191-5. Journal code: 101131136. ISSN: 1536-8599. Pub. country: United States. Language: English.
AB In this study we produced a recombinant human Tartrate-resistant acid phosphatase (TRAP) enzyme from baculovirus-infected insect cells, generated four monoclonal **antibodies** (MAbs) 15A4, 13B9, **1C6** and 3G7, to the enzyme, and characterized these **antibodies**. In the human serum and lung specimen, all four **antibodies** appeared to have a high specificity for native TRAP enzyme in western blot analysis, immunohistochemical analysis and enzyme immunoassay. These **antibodies** may react with respective conformational determinants, therefore, they may be useful for detection of active TRAP. Only one of the **antibodies**, 15A4 also reacted with a denatured epitope, therefore, it is suitable for western blot analysis, enzyme immunoassay and for immunohistochemistry in the rat. Taken together, having characterized properties of four monoclonal **antibodies** against recombinant human TRAP enzyme may be useful for development of TRAP specific immunoassays in pathology and hematology of the bone. They will certainly be of use for the study of biosynthesis, regulation and function of the TRAP enzyme.

L3 ANSWER 10 OF 55 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
2002:549344 The Genuine Article (R) Number: 568QY. Characterization of four monoclonal **antibodies** to recombinant human Tartrate-resistant acid phosphatase. Miyazaki T (Reprint); Matsunaga T; Miyazaki S; Hokari S; Komoda T. Saitama Med Sch, Dept Biochem, 38 Morohongo, Moroyama, Saitama 3500495, Japan (Reprint); Saitama Med Sch, Dept Biochem, Moroyama, Saitama 3500495, Japan; Yamasa Corp, Immunol Lab, Chiba 2880056, Japan. HYBRIDOMA AND HYBRIDOMICS (JUN 2002) Vol. 21, No. 3, pp. 191-195. Publisher: MARY ANN LIEBERT INC PUBL. 2 MADISON AVENUE, LARCHMONT, NY 10538 USA. ISSN: 0272-457X. Pub. country: Japan. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB In this study we produced a recombinant human Tartrate-resistant acid phosphatase (TRAP) enzyme from baculovirus-infected insect cells, generated four monoclonal **antibodies** (MAbs) 15A4, 13139, **1C6** and 3G7, to the enzyme, and characterized these **antibodies**. In the human serum and lung specimen, all four **antibodies** appeared to have a high specificity for native TRAP enzyme in western blot analysis, immunohistochemical analysis and enzyme immunoassay. These **antibodies** may react with respective conformational determinants, therefore, they may be useful for detection of active TRAP. Only one of the **antibodies**, 15A4 also reacted with a denatured epitope, therefore, it is suitable for western blot analysis, enzyme immunoassay and for immunohistochemistry in the rat. Taken together, having characterized properties of four monoclonal **antibodies** against recombinant human TRAP enzyme may be useful for development of TRAP specific immunoassays in pathology and hematology of

the bone. They will certainly be of use for the study of biosynthesis, regulation and function of the TRAP enzyme.

L3 ANSWER 11 OF 55 MEDLINE on STN DUPLICATE 6
2002441953 Document Number: 22187506. PubMed ID: 12199521. Improvements in the measurement of stool decay-accelerating factor in the detection of colorectal cancer. Ohya Shogen; Mizuno Motowo; Kawada Mikihiro; Nasu Junichirou; Okada Hiroyuki; Shimomura Hiroyuki; Yamamoto Kazuhide; Fujita Teizo; Tsuji Takao. (Department of Medicine and Medical Science, Okayama University Graduate School of Medicine and Dentistry, Japan.) ACTA MEDICA OKAYAMA, (2002 Aug) 56 (4) 171-6. Journal code: 0417611. ISSN: 0386-300X. Pub. country: Japan. Language: English.

AB We have previously developed an enzyme-linked immunosorbent assay (ELISA) to measure stool decay-accelerating factor (DAF) and found that stool DAF concentrations were significantly elevated in patients with colorectal cancer, suggesting that the measurement of stool DAF may be valuable for the detection of colorectal cancer. In order to refine the assay for the measurement of stool DAF, we investigated 1) effects of centrifugation of stool samples, 2) effects of detergents, and 3) adequate combination of various anti-DAF monoclonal **antibodies** for the ELISA system using only monoclonal **antibodies**. We found that high-speed centrifugation could be omitted and that only the removal of large undigested food residues by centrifugation of short duration in a low-speed benchtop microcentrifuge sufficed to adequately prepare the stool samples. Addition of 2 detergents, octyl beta-glucoside and sodium deoxycholate, known to solubilize glycosyl-phosphatidylinositol-anchored proteins such as DAF, did not influence stool DAF values. By using 2 mouse anti-DAF monoclonal **antibodies** (clone 4F11 and **1C6**), we were able to achieve a stable ELISA for the measurement of stool DAF using a uniform source of **antibodies**. The results should allow us to consistently apply the DAF assay for routine use in the detection of colorectal cancer.

L3 ANSWER 12 OF 55 CAPLUS COPYRIGHT 2003 ACS on STN
2002:912980 Document No. 138:269328 Clinical Significance of Angiogenic Factor Expression at the Deepest Invasive Site of Advanced Colorectal Carcinoma. Kaio, Eijiro; Tanaka, Shinji; Kitadai, Yasuhiko; Sumii, Masaharu; Yoshihara, Masaharu; Haruma, Ken; Chayama, Kazuaki (The First Department of Internal Medicine, Hiroshima University School of Medicine, Hiroshima, Japan). Oncology, Volume Date 2003, 64(1), 61-73 (English) 2002. CODEN: ONCOBS. ISSN: 0030-2414. Publisher: S. Karger AG.

AB Tumor angiogenesis is a complicated process for which the mechanisms remain unclear. The aim of this study was to elucidate the clin. significance of several angiogenic factor expression as a predictor of the invasive/metastatic potential and of the prognosis of advanced colorectal carcinoma (CRC) in relation to their intratumoral histol. heterogeneity. One hundred fifty two patients who had undergone surgical resection for advanced CRC entered this study. PD-ECGF, VEGF, and VEGF-C were examd. immunohistochem. with **antibodies** **1C6**-203, A-20, and C-20, resp. Tumor microvessel d. (MVD) was detd. immunohistochem. with anti-CD34 **antibody**. Expression of PD-ECGF, of VEGF, and of VEGF-C at the deepest invasive site were detected in 77 (50.7%), 62 (30.8%), and 71 (46.7%) of the 152 lesions, resp. PD-ECGF, VEGF, and VEGF-C expression at the deepest invasive site in lesions with liver metastasis (77, 67, and 70%) was significantly higher than that in those without liver metastasis (44, 34, and 41%). In cases with curative surgery, patients with PD-ECGF, VEGF, and VEGF-C expression at the deepest invasive site had a significantly poorer prognosis than those without PD-ECGF, VEGF, and VEGF-C expression at the deepest invasive site. PD-ECGF, VEGF, and VEGF-C expression at the deepest invasive site correlated significantly with MVD. Multivariate anal. with logistic regression for 5-yr survival in patients with curative surgery showed that lymph node metastasis and VEGF expression were significant risk factors. Expression of PD-ECGF, VEGF, and VEGF-C was correlated significantly with

metastatic potential and prognosis in relation to MVD. Of the several angiogenic factors, VEGF expression at the deepest invasive site of tumor was the most statistically significant indicator of prognosis in advanced CRC.

L3 ANSWER 13 OF 55 CAPLUS COPYRIGHT 2003 ACS on STN
2001:91532 Document No. 134:146406 Cloning and characterization of the human CXCR3 receptor. Loetscher, Marcel; Moser, Bernhard; Qin, Shixin; Mackay, Charles R. (Millennium Pharmaceuticals, Inc., USA; Theodor-Kocher Institute). U.S. US 6184358 B1 20010206, 49 pp., Cont.-in-part of U.S. Ser. No. 709,838. (English). CODEN: USXXAM. APPLICATION: US 1997-829839 19970331. PRIORITY: US 1996-709838 19960910.
AB The authors disclose the cloning of human CXC chemokine Receptor 3 (CXCR3). CXCR3 was shown to be expressed by activated/memory T-cells and to be functional in chemotaxis assays using IP-10 and Mig chemokines. In addn., **antibodies** reactive with CXCR3 were produced; one clone (designated **1C6**) was shown to inhibit the response to IP-10 but not that of Mig.

L3 ANSWER 14 OF 55 MEDLINE on STN DUPLICATE 7
2001080979 Document Number: 20569277. PubMed ID: 11118485. Development and characterization of **1C6**-203, a new monoclonal **antibody** specific to human thymidine phosphorylase. Kono T; Nishida M; Inagaki N; Tanaka Y; Yoneda M; Kasai S. (Second Department of Surgery and Medicine, Kamakura, Kanagawa, Japan.. kono@asahikawa-med.ac.jp) . JOURNAL OF HISTOCHEMISTRY AND CYTOCHEMISTRY, (2001 Jan) 49 (1) 131-8. Journal code: 9815334. ISSN: 0022-1554. Pub. country: United States. Language: English.
AB Thymidine phosphorylase (dThdPase) is an essential enzyme for activation of the oral cytostatic drug capecitabine and its intermediate metabolite, doxifluridine, to 5-fluorouracil in tumors. Methods to estimate dThdPase expression in tumor tissue might be useful to predict the efficacy of capecitabine and doxifluridine in cancer patients. We established a new monoclonal **antibody** (MAb), **1C6**-203, applicable for dThdPase immunohistochemistry and compared its staining characteristics with those of a previously established MAb, 654-1. In 4% paraformaldehyde-fixed colorectal carcinoma, **1C6**-203 and 654-1 stained cancer cells in 19/30 and 9/30 patients, respectively. In 10% formalin-fixed colorectal carcinoma, **1C6**-203 and 654-1 stained cancer cells in 18/30 and 6/30 patients, respectively. In negative 10% formalin-fixed tissues, microwave treatment improved the positivity of 654-1-stained cancer cells. These results suggest that an epitope recognized by **1C6**-203 is resistant to epitope masking by formaldehyde fixation, whereas that for MAb 654-1 is sensitive. Therefore, MAb **1C6**-203 might be more suitable than MAb 654-1 for evaluating dThdPase expression in colorectal carcinoma.

L3 ANSWER 15 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
2000:515173 Document No.: PREV200000515173. Mab reactions with various B cell lines and tonsil cells. Sun, Y. X. [Reprint author]; Chen, Y. [Reprint author]; Shen, B. F. [Reprint author]. Department of Molecular Immunology, Institute of Basic Medical Science, Beijing, China. Tissue Antigens, (2000) Vol. 55, No. Supplement 1, pp. 36. print.
Meeting Info.: 7th Workshop and Conference on Human Leucocyte Differentiation Antigens. Harrogate, England, UK. June 20-24, 2000.
CODEN: TSANA2. ISSN: 0001-2815. Language: English.

L3 ANSWER 16 OF 55 MEDLINE on STN DUPLICATE 8
1999272784 Document Number: 99272784. PubMed ID: 10339663. Retroviruses prepared from human DAF expressing murine packaging cells acquire resistance against human serum. Hiasa A; Watanabe M; Okada H; Ikenaka K; Fujita T; Yoshimatsu T; Kanematsu T; Shiku H. (Second Department of Internal Medicine, Mie University School of Medicine, Tsu, Mie 514-8507, Japan.) INTERNATIONAL JOURNAL OF ONCOLOGY, (1999 Jun) 14 (6) 1091-6.

Journal code: 9306042. ISSN: 1019-6439. Pub. country: Greece. Language: English.

AB The complement system of the human body inactivates the infectious ability of retroviruses injected as an artificial gene transfer vector. We established new murine leukemia virus (MuLV) packaging cell lines; D2SS and D7S which express decay-accelerating factor (DAF) on their surface. Both D2SS and D7S were resistant against incubation with fresh human serum. Moreover, the retroviruses produced from these packaging cell lines were also resistant to serum treatment. This resistance can be inhibited by DAF neutralizing **antibody 1C6**. These data demostrate that DAF induces a partial protection of MuLV infection from the human complement system.

L3 ANSWER 17 OF 55 CAPLUS COPYRIGHT 2003 ACS on STN

1998:184011 Document No. 128:242903 Human CXC chemokine receptor 3, its cDNA sequence, and its diagnostic and therapeutic uses. Loetscher, Marcel; Moser, Bernhard; Qin, Shixin; Mackay, Charles R. (Theodor-Kocher Institute, Switz.; Leukosite, Inc.). PCT Int. Appl. WO 9811218 A1 19980319, 137 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US15915 19970910. PRIORITY: US 1996-709838 19960910; US 1997-829839 19970331.

AB The present invention relates to recombinant chemokine designated CXC Chemokine Receptor 3 (CXCR3) that is selective for the CXC chemokines IP-10 (interferon .gamma.-inducible 10-kDa protein) and Mig (monokine induced by .gamma.-interferon), and/or the ability to induce a cellular response (e.g., chemotaxis, exocytosis). The cDNA clone which was isolated from a human CD4+ T cell library, was not detected in monocyte- or granulocyte-derived cDNA libraries. Sequence anal. of the clone revealed an open reading frame of 1104 bp, encoding a predicted protein of 368 amino acids with a predicted mol. mass of 40,659 Da. The amino acid sequence includes 7 putative transmembrane segments which are characteristic of G-protein coupled receptors and are found in other chemoattractant receptors. Consistent with this observation, the receptor mediates Ca2+ mobilization and chemotaxis in response to IP-10 and Mig. Lymphocytes, particularly T lymphocytes, bearing a CXCR3 receptor as a result of activation can be recruited into inflammatory lesions, sites of infection, or tumors by IP-10 and/or Mig, which can be induced locally by interferon-.gamma.. Thus, CXCR3 plays a role in the selective recruitment of lymphocytes, particularly effector cells such as activated or stimulated T lymphocytes. Another aspect of the invention relates to antisense nucleic acid, recombinant nucleic acid constructs, such as plasmids or retroviral vectors, methods of identifying ligands, and inhibitors (e.g., antagonists) or promoters (e.g., agonists) of receptor function.

L3 ANSWER 18 OF 55 MEDLINE on STN DUPLICATE 9

1998281913 Document Number: 98281913. PubMed ID: 9620603. Signal transduction via a protein associated with a glycosylphosphatidylinositol-anchored protein, decay-accelerating factor (DAF/CD55). Kuraya M; Fujita T. (Department of Biochemistry, Fukushima Medical College, Japan.) INTERNATIONAL IMMUNOLOGY, (1998 Apr) 10 (4) 473-80. Journal code: 8916182. ISSN: 0953-8178. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Decay-accelerating factor (DAF/CD55) is a glycosylphosphatidylinositol-anchored protein which is known to have signal transducing capacity and to be associated with several proteins. To determine the signal transducer in the DAF-forming complex, we purified DAF-associated proteins from Raji B cells using an anti-DAF mAb (**1C6**)-bound affinity column and

established five mAb against them. Among these, mAb 2E12-G7(IgM/kappa) reacted with a variety of intact cells, including peripheral blood mononuclear cells (PBMC), as well as cells from T and B cell lines, as shown by cytofluorimetric analyses. The Mr of 2E12-G7 antigen was estimated to be 43 kDa by surface biotinylation and immunoblotting analysis. This antigen was demonstrated in **1C6** immunoprecipitates, but not in anti-CD59 (another GPI-anchored complement regulatory factor)-immunoprecipitates. Sequential treatment with **1C6** F(ab')2 and then with anti-mouse Ig F(ab')2 stimulated PBMC to induce tyrosine phosphorylation on proteins of 45, 72, 78 and approximately 100 kDa. Also, mAb cross-linked to 2E12-G7 stimulated PBMC to induce tyrosine phosphorylation on proteins of 72, 78 and approximately 100 kDa. Furthermore, when 2E12-G7 and **1C6** immunoprecipitates were incubated with [gamma-32P]ATP, the main constituents detected in both were phosphorylated proteins of 26, 32 and 62 kDa. Thus, DAF-associated 2E12-G7 antigen transduces a signal, similar to the DAF molecule.

L3 ANSWER 19 OF 55 MEDLINE on STN DUPLICATE 10

1998327276 Document Number: 98327276. PubMed ID: 9662774. Changes in third carpal bone articular cartilage after synovectomy in normal and inflamed joints. Palmer J L; Bertone A L; Malemud C J; Mansour J. (Department of Veterinary Clinical Sciences, Ohio State University, Columbus, USA.) VETERINARY SURGERY, (1998 Jul-Aug) 27 (4) 321-30. Journal code: 8113214. ISSN: 0161-3499. Pub. country: United States. Language: English.

AB OBJECTIVE: To determine if arthroscopic synovectomy in normal and inflamed joints had temporal or site-related effects on articular cartilage. STUDY DESIGN: Alterations in equine third carpal bone articular cartilage were studied at two time periods: groups 1 and 2 (6 weeks) and groups 3 and 4 (2 weeks) after synovectomy in normal (groups 2 and 4) and inflamed carpi (groups 1 and 3). ANIMAL POPULATION: 16 carpi from eight horses. METHODS: Biochemical and biomechanical properties of dorsal and palmar articular cartilage were determined by radioloabeling, proteoglycan (PG) extraction, chromatography, electrophoresis, and indentation testing. RESULTS: Synovectomy in inflamed joints produced the greatest concentration of newly synthesized PG in articular cartilage by 2 weeks. Synovectomy in normal joints produced significantly greater newly synthesized PG in articular cartilage by 6 weeks. Dorsal sites had greater newly synthesized and endogenous PG in some groups. Chromatographic profiles of newly synthesized PG demonstrated early and late PG peaks. Electrophoresis of late PG peak showed a toluidine blue-positive band that comigrated with human A1D1 PG monomer in the two groups with the most newly synthesized PG> This band was reactive with monoclonal **antibody 1C6** specific for the hyaluronic acid-binding region of aggrecan. For the material properties evaluated, only Poisson's ratio was significantly decreased between groups as a function of time (6 weeks < 2 weeks). and this was most pronounced in the thicker dorsal sites. CONCLUSIONS: Synovectomy in inflamed joints produced site-specific, significantly greater responses in articular cartilage as compared with synovectomy in normal joints. CLINICAL RELEVANCE: Synovectomy may not be beneficial to the articular cartilage in inflamed joints.

L3 ANSWER 20 OF 55 MEDLINE on STN DUPLICATE 11

96312531 Document Number: 96312531. PubMed ID: 8700877. T-cell epitope analysis using subtracted expression libraries (TEASEL): application to a 38-kDA autoantigen recognized by T cells from an insulin-dependent diabetic patient. Neophytou P I; Roep B O; Arden S D; Muir E M; Duinkerken G; Kallan A; de Vries R R; Hutton J C. (Department of Clinical Biochemistry, University of Cambridge, Addenbrooke's Hospital, United Kingdom.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Mar 5) 93 (5) 2014-8. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Studies on circulating T cells and **antibodies** in newly diagnosed

type 1 diabetic patients and rodent models of autoimmune diabetes suggest that beta-cell membrane proteins of 38 kDa may be important molecular targets of autoimmune attack. Biochemical approaches to the isolation and identification of the 38-kDa autoantigen have been hampered by the restricted availability of islet tissue and the low abundance of the protein. A procedure of epitope analysis for CD4+ T cells using subtracted expression libraries (TEASEL) was developed and used to clone a 70-amino acid pancreatic beta-cell peptide incorporating an epitope recognized by a 38-kDa-reactive CD4+ T-cell clone (**1C6**) isolated from a human diabetic patient. The minimal epitope was mapped to a 10-amino acid synthetic peptide containing a DR1 consensus binding motif. Data base searches did not reveal the identity of the protein, though a weak homology to the bacterial superantigens SEA (Streptococcus pyogenes exotoxin A) and SEB (Staphylococcus aureus enterotoxin B) (23% identity) was evident. The TEASEL procedure might be used to identify epitopes of other autoantigens recognized by CD4+ T cells in diabetes as well as be more generally applicable to the study low-abundance autoantigens in other tissue-specific autoimmune diseases.

L3 ANSWER 21 OF 55 MEDLINE on STN

96149186 Document Number: 96149186. PubMed ID: 8567980. Imogen 38: a novel 38-kD islet mitochondrial autoantigen recognized by T cells from a newly diagnosed type 1 diabetic patient. Arden S D; Roep B O; Neophytou P I; Usac E F; Duinkerken G; de Vries R R; Hutton J C. (Department of Clinical Biochemistry, University of Cambridge, Addenbrooke's Hospital, United Kingdom.) JOURNAL OF CLINICAL INVESTIGATION, (1996 Jan 15) 97 (2) 551-61. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB Cell-mediated autoimmune attack directed against islet proteins of approximately 38 kD in size has been associated with type 1 diabetes. A novel murine cDNA encoding an antigen of this size was cloned using a screening procedure based on the proliferative response of a human diabetic T cell clone (**1C6**) to a recombinant antigen epitope library. Membrane preparations from COS 7 cells transfected with the full-length 1,267-bp cDNA elicited a proliferative response from the reporter T cells comparable to that of the defined peptide epitope and native insulinoma antigen. In vitro translation and transfection experiments suggested that the protein is initially synthesized as a 44-kD protein and then processed to the native 38-kD form through the proteolytic removal of a 54-aa NH2-terminal mitochondrial targeting sequence. Differential centrifugation, Percoll density gradient centrifugation, and immunofluorescence studies confirmed localization of the antigen to mitochondria. Northern blot, Western blot, and **1C6** T cell proliferation assays showed that, although imogen 38 was more highly expressed in beta cell than alpha cell lines, it was also present in other tissues. It is concluded that imogen 38 may be a target for bystander autoimmune attack in diabetes rather than a primary autoantigen.

L3 ANSWER 22 OF 55 CAPLUS COPYRIGHT 2003 ACS on STN

1997:295400 Document No. 126:316466 Establishment and preliminary application of McAb-CIEIA for determination of zearalenone. Lu, Ge; Liu, Chunxia; Ji, Rong (Beijing Res. Inst. Nutritional Resources, Beijing, 100054, Peop. Rep. China). Zhenjun Xuebao, 15(4), 292-296 (Chinese) 1996. CODEN: ZHXUET. ISSN: 0256-1883. Publisher: Kexue.

AB A hybridoma cell line secreting McAb against zearalenone (ZEN) was established by fusion of Sp-2/0-Ag-14 and spleen cells from BALB/c mice immunized with ZEN-BSA conjugate. The McAb, designated AEN-**1C6**, was of the subtype IgG1 and the ascitic fluid content was 10-5 by indirect ELISA. The cross-reactivities of this McAb for zearalanone, .alpha.-zearalanol, .beta.-zearalenol, .alpha.-zearalanol, and .beta.-zearalanol were 1.20, 1.14, 0.16, 1.03 and 0.40%, resp. of that for ZEN. An competitive inhibition enzyme immunoassay (CIEIA) was developed for the detection of ZEN in food (including corn, wheat and rice) using ZEN-**1C6**. The linear range for ZEN by the method was 5-1000

ng/mL and the detection limit was 0.1 ng/mL. The mean recovery rates were 84.0-105.5%. A total of 81 samples collected from market were analyzed with the CIEIA, and the concn. of ZEN ranges from 0.2-125.8 .mu.g/kg.

L3 ANSWER 23 OF 55 MEDLINE on STN DUPLICATE 12

96399656 Document Number: 96399656. PubMed ID: 8806114. Biochemical and biomechanical alterations in equine articular cartilage following an experimentally-induced synovitis. Palmer J L; Bertone A L; Malemud C J; Mansour J. (Department of Veterinary Clinical Sciences, Ohio State University, Colombus, USA.) OSTEOARTHRITIS AND CARTILAGE, (1996 Jun) 4 (2) 127-37. Journal code: 9305697. ISSN: 1063-4584. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The effects of inflammation on the biochemical and biomechanical properties of articular cartilage at two sites (dorsal and palmar) from the radial facet of the equine third carpal bone were examined in response to a synovitis induced with Escherichia coli lipopolysaccharide (LPS). Four groups were studied. In group 1 synovitis was induced at time zero and evaluated at week 6. Group 2 was the sham-treated control for group 1. In group 3 synovitis was induced at time zero and evaluated at week 2. Group 4 was the sham-treated control for group 3. There was a significant increase ($P < 0.05$) in newly synthesized proteoglycan PG from both sites in group 3 as compared to the sham-treated groups and group 1. No significant difference in the endogenous PG concentration between groups or sites was detected. Sepharose CL-2B revealed two peaks of newly synthesized PG in all groups; an early peak (Kav 0.11-0.13) and a late peak (Kav 0.48-0.64). Newly synthesized PG profiles from sham-treated groups and group 3 were similar, but the group 3 PG profile exhibited a more pronounced early peak. Conversely, the PG profile from group 1 demonstrated a more prominent late peak. Electrophoresis and Western blot analysis of the pooled late PG peak fractions from the sham-treated and group 1 showed a single toluidine blue stained band from both sites which reacted with monoclonal **antibody** (MAb) **1C6**. By contrast, the late peak from the palmar site in group 3 showed an additional faster moving component on composite gels which did not react with MAb **1C6**. There was a significant decrease in Poisson's ratio and a significant increase in cartilage thickness in groups 1 and 3 which had received synovitis. The increase in cartilage thickness of groups 1 and 3 was also significantly affected by site (dorsal > palmar). There was no significant difference in aggregate modulus or permeability constant among groups. Primary joint inflammation induced by LPS alters the biochemical and biomechanical properties of the articular cartilage as a function of time and site. An increase in chondrocyte PG synthesis in the early period following synovitis may be a reparative response to the inflammatory insult. Continued alterations in the qualitative PG composition in the later period following synovitis may represent a shift in chondrocyte metabolism to repopulate the existing cartilage matrix.

L3 ANSWER 24 OF 55 MEDLINE on STN DUPLICATE 13

96167406 Document Number: 96167406. PubMed ID: 8599516. Site-specific proteoglycan characteristics of third carpal articular cartilage in exercised and nonexercised horses. Palmer J L; Bertone A L; Malemud C J; Carter B G; Papay R S; Mansour J. (Department of Veterinary Clinical Sciences, Ohio State University, Columbus 43210, USA.) AMERICAN JOURNAL OF VETERINARY RESEARCH, (1995 Dec) 56 (12) 1570-6. Journal code: 0375011. ISSN: 0002-9645. Pub. country: United States. Language: English.

AB The relevance of site and the influence of exercise on third carpal articular cartilage proteoglycan (PG) were assessed in 16 horses. Six horses were exercised (exercised group) for 30 minutes, 3 times/wk, for 6 weeks. The other 10 horses (nonexercised group) were housed in box stalls for the same 6-week period. At week 6, articular cartilage from the proximal surface of the right third carpal bone was harvested and cultured with radioactive sulfate to label newly synthesized PG. Endogenous PG was measured by use of a uronic acid assay. Newly synthesized and endogenous PG were characterized by use of Sepharose CL-2B chromatography, composite

gel electrophoresis, and/or immunoblot analysis with monoclonal **antibody 1C6** directed against the hyaluronic acid-binding region on PG. There was a significant (P = 0.0002) effect of exercise, but not site, on newly synthesized PG, which was increased in the exercised horses, compared with the nonexercised horses at the end of the 6-week study period. The increase in newly synthesized PG was not reflected in the existing cartilage matrix as there was no significant difference between groups in endogenous PG. However, there was a significant (P = 0.01) effect of site on endogenous PG, with the nest of sites located in the palmar aspect of the radial facet containing a greater concentration of endogenous PG than the nests of sites located on the dorsal aspect of the radial facet or all sites on the intermediate facet. Most newly synthesized PG in both groups consisted of hydrodynamically small PG monomers. However, there was a change in the profile of newly synthesized PG at some sites in the exercised horses to include an early elution peak on Sepharose CL-2B, which may contain aggregating PG. All sites in both groups contained a diverse population of endogenous large and small PG on toluidine blue-stained composite gels that reacted with monoclonal **antibody 1C6**, indicating the potential to bind to hyaluronic acid.

L3 ANSWER 25 OF 55 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
96:86476 The Genuine Article (R) Number: TQ281. BETA-CELL REACTIVE T-CELL CLONES FROM TYPE-I DIABETES PATIENTS ARE NOT BETA-CELL SPECIFIC AND RECOGNIZE MULTIPLE ANTIGENS. KALLAN A A (Reprint); ROEP B O; ARDEN S D; HUTTON J C; DEVRIES R R P. ACAD HOSP LEIDEN, DEPT IMMUNOHEMATOL, BLDG 1, E3-Q, RIJNSBURGERWEG 10, 2333 AA LEIDEN, NETHERLANDS (Reprint); UNIV LEIDEN HOSP, DEPT IMMUNOHEMATOL, 2300 RC LEIDEN, NETHERLANDS; UNIV LEIDEN HOSP, BLOOD BANK, 2300 RC LEIDEN, NETHERLANDS; UNIV CAMBRIDGE, ADDENBROOKES HOSP, DEPT CLIN BIOCHEM, CAMBRIDGE, ENGLAND. JOURNAL OF AUTOIMMUNITY (DEC 1995) Vol. 8, No. 6, pp. 887-899. ISSN: 0896-8411. Pub. country: NETHERLANDS; ENGLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Type I diabetes is the result of an autoimmune destruction of pancreatic beta cells. T cells appear to play a key role in this process. Thus far little information is available on the beta cell antigen or antigens recognized by auto-reactive T cells. Previously, we identified a 38 kD T cell antigen that appears to be localized in the membrane ofinsulin secretory granules and that is recognized by T cells from newly diagnosed type I diabetes patients. Other groups have reported T cell reactivity against glutamic acid decarboxylase (GAD). To obtain an indication of whether or not beta-cell reactive T cells from type I diabetes patients recognize a Limited number of beta-cell antigens, we cloned T-cell lines reactive with rat insulinoma (RIN) membranes from two patients and analysed their antigen specificity. We also studied the antigen specificity of one RIN membrane reactive T-cell clone (1C5), previously isolated from a third patient. From the first patient two identical RIN membrane reactive T-cell clones (7A13) were isolated. The second patient yielded two identical (23A19) RIN membrane reactive T-cell clones, and one that was different (234A33). All clones were CD4(+) and saw antigen in the context of different HLA class II alleles. The reactivity of the clones was, however, not restricted to beta cells: all clones showed cross-reactivity with one or more rat tissues, with some preference for those of neuroendocrine origin, but the cross-reactivity patterns were all different. All four clones recognized different fractions electro-eluted from RIN membranes: 29-36 kDa (7A13), 120-170 (23A19), 29-41 (23A33) and 56-72kDa (1C5). The 23A33 clone reacted with the same 38 kDa fraction electro-eluted from insulinoma membranes as a beta-cell reactive clone (**1C6**) published previously, but none of the other known beta cell antigen preparations tested were recognized by the T-cell clones. Finally, the subcellular localization of the antigens recognized showed at least two different patterns. These data indicate that beta-cell reactive T cells from the peripheral blood of type I diabetes patients are not necessarily beta-cell specific and may be

heterogeneous in regard to their antigen specificity and HLA class II restriction. (C) 1995 Academic Press Limited

L3 ANSWER 26 OF 55 MEDLINE on STN DUPLICATE 14
96027644 Document Number: 96027644. PubMed ID: 8547061. Homologous restriction of complement-mediated cell lysis can be markedly enhanced by blocking decay-accelerating factor. Zhong R K; Kozii R; Ball E D. (Division of Hematology/Bone Marrow Transplantation, University of Pittsburgh Medical Center, PA 15213, USA.) BRITISH JOURNAL OF HAEMATOLOGY, (1995 Oct) 91 (2) 269-74. Journal code: 0372544. ISSN: 0007-1048. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Regulation of complement (C') dependent lysis of cells is attributed to certain membrane proteins. One of these is decay-accelerating factor (DAF), CD55, a 70kD glycosylated protein which functions to protect host cells from damage by autologous C'. We hypothesized that blockade of DAF function by a monoclonal **antibody** (mAb) could augment C'-dependent lysis mediated by another mAb to a cell surface antigen expressed on leukaemia cells. Thus, we tested the effects of the anti-DAF mAb **1C6** on the ability of both rabbit and human C' to lyse human leukaemia cells through activation by complement-fixing murine mAb. DAF antigen was highly expressed on most leukaemia cell lines and primary acute leukaemia blast cells tested. Murine mAb to CD15 (PM-81) and to gp 120 (AML-1-99), both IgM, also bound to the majority of myeloid and lymphoid leukaemia cells. Using human serum as a source of C', the addition of mAb **1C6** reduced by an additional 85-94% the numbers of clonogenic HL-60 (myeloid leukaemia) cells lysed by mAb PM-81 alone. Similarly, the addition of mAb **1C6** reduced by an additional 87% the numbers of HL-60 colonies eliminated by mAb AML-1-99 alone. Similar results were observed in an experimental purging model using the myeloid leukaemia cell lines HL-60, U937 or NB4 cells as targets. These results show that mAb **1C6** can effectively block the actions of DAF. In the presence of mAb **1C6**, the cytotoxic activity mediated by human C' was similar to that of rabbit C'. These results show that increased tumour cell killing can be achieved through DAF blockade. This finding has relevance to clinical trials using C'-fixing mAb for purging bone marrow of occult tumour cells prior to autologous transplantation.

L3 ANSWER 27 OF 55 MEDLINE on STN DUPLICATE 15
94175901 Document Number: 94175901. PubMed ID: 8129731. Identity of the core proteins of the large chondroitin sulphate proteoglycans synthesized by skeletal muscle and prechondrogenic mesenchyme. Carrino D A; Dennis J E; Drushel R F; Haynesworth S E; Caplan A I. (Department of Biology, Case Western Reserve University, Cleveland, OH 44106-7080.) BIOCHEMICAL JOURNAL, (1994 Feb 15) 298 (Pt 1) 51-60. Journal code: 2984726R. ISSN: 0264-6021. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Large, chondroitin sulphate-containing proteoglycans are synthesized by three prominent tissue in the embryonic chick limb. One of these proteoglycans is aggrecan, the phenotype-specific proteoglycan of cartilage. Another, PG-M, is produced by prechondrogenic mesenchymal cells. The third, M-CSPG, is made by developing skeletal muscle cells. While the carbohydrate components of PG-M and M-CSPG share some similarities, both of these proteoglycans clearly have different carbohydrate moieties from those of aggrecan. To compare these three proteoglycans at another level, their core protein structures were analysed in three ways: by the presence or absence of monoclonal **antibody** epitopes, by one-dimensional peptide display of the cyanogen bromide-cleaved core proteins and by electron microscopic imaging of the molecules. Monoclonal **antibodies** whose epitopes are present in aggrecan core protein were tested with core protein preparations from M-CSPG and PG-M. One of these, 7D1, recognizes both PG-M and M-CSPG, while another, **1C6**, shows no reactivity for the non-cartilage proteoglycans. The absence of **1C6** reactivity is of interest, as its epitope is in a region of the aggrecan core protein known to have a functional homologue in the core proteins of PG-M and

M-CSPG. The cyanogen bromide-fragmented peptide pattern of M-CSPG is the same as that of PG-M, and both are different from that of aggrecan. The aggrecan pattern has one prominent large band (molecular mass 130 kDa), some less prominent large bands (molecular mass 70-100 kDa) and several smaller bands. In contrast, the PG-M and M-CSPG patterns show no bands with molecular masses > 73 kDa, and the smaller bands (molecular mass < 40 kDa) have a different pattern to that of the smaller bands from aggrecan. The electron microscopic images of aggrecan show a core protein with one end having two globular regions separated by a short linear segment; adjacent to this is a long linear segment, which sometimes contains a third globular region at the end of the core protein opposite the end with the double-globe structure. M-CSPG and PG-M core proteins never show images with the double-globe structure. Instead, one end of the molecule has a single globular domain, and a second globular region is variably present at the opposite end of the core protein. Thus, by all three methods, the core proteins of PG-M and M-CSPG appear to be the same and both differ from the core protein of aggrecan.

L3 ANSWER 28 OF 55 CAPLUS COPYRIGHT 2003 ACS on STN

1994:213024 Document No. 120:213024 Identity of the core proteins of the large chondroitin sulfate proteoglycans synthesized by skeletal muscle and prechondrogenic mesenchyme. Carrino, David A.; Dennis, James E.; Drushel, Richard F.; Haynesworth, Stephen E.; Caplan, Arnold I. (Skeletal Res. Cent., Case West. Reserve Univ., Cleveland, OH, 44106-7080, USA). Biochemical Journal, 298(1), 51-60 (English) 1994. CODEN: BIJOAK. ISSN: 0306-3275.

AB Large, chondroitin sulfate-contg. proteoglycans are synthesized by three prominent tissues in the embryonic chick limb. One of these proteoglycans is aggrecan, the phenotype-specific proteoglycan of cartilage. Another, PG-M, is produced by prechondrogenic mesenchymal cells. While the carbohydrate components of PG-M and M-CSPG share come similarities, both of these proteoglycans clearly have different carbohydrate moieties from those of aggrecan. To compare these three proteoglycans at another level, their core protein structures were analyzed in three ways: by the presence or absence of monoclonal **antibody** epitopes, by one-dimensional peptide display of the cyanogen bromide-cleaved core proteins and by electron microscopic imaging of the mols. Monoclonal **antibodies** whose epitopes are present in aggrecan core protein were tested with core protein prepns. from M-CSPG and PG-M. One of these, 7D1, recognizes both Pg-M and M-CSPG, while another, **1C6**, shows no reactivity for the non-cartilage proteoglycans. The absence of **1C6** reactivity is of interest, as its epitope is in a region of the aggrecan core protein known to have a functional homolog in the core proteins of PG-M and M-CSPG. The cyanogen bromide-fragmented peptide pattern of M-CSPG is the same as that of PG-M, and both are different from that of aggrecan. The aggrecan pattern has one prominent large band (mol. mass 130 kDa), some less prominent large bands (mol. mass 70-100 kDa) and several smaller bands. In contrast, the PG-M and M-CSPG patterns show no bands with mol. masses > 73 kDa, and the smaller bands (mol. mass < 40 kDa) have a different pattern to that of the smaller bands from aggrecan. The electron microscopic images of aggrecan show a core protein with one end having two globular regions sepd. by a short linear segment; adjacent to this is a long linear segment, which sometimes contains a third globular region at the end of the core protein opposite the end with the double-globe structure. M-DSPG and PG-M core proteins never show images with the double-globe structure. Instead, one end of the mol. has a single globular domain, and a second globular region is variably present at the opposite end of the core protein. Thus, by all three methods, the core proteins of PG-M and M-CSPG appear to be the same and both differ from the core protein of aggrecan.

L3 ANSWER 29 OF 55 MEDLINE on STN DUPLICATE 16

94014343 Document Number: 94014343. PubMed ID: 8409382. Immune functions of tumor necrosis factor. I. Tumor necrosis factor induces apoptosis of

mouse thymocytes and can also stimulate or inhibit IL-6-induced proliferation depending on the concentration of mitogenic costimulation. Hernandez-Caselles T; Stutman O. (Immunology Program, Memorial Sloan-Kettering Cancer Center, New York, NY 10021.) JOURNAL OF IMMUNOLOGY, (1993 Oct 15) 151 (8) 3999-4012. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Murine rTNF produces at least three effects on mouse thymocytes in vitro: 1) Is a modest co-stimulator of proliferation with low PHA-P doses. 2) Has a bi-directional interaction with rIL-6-depending on PHA concentration: at low PHA (5 to 10 micrograms/ml) TNF augments and at high PHA (20 to 30 micrograms/ml) inhibits IL-6-induced proliferation. A comparable bidirectional PHA dose-dependent TNF interaction was seen with IL-1 beta, whereas only inhibition at high PHA with IL-2 and only augmentation at low PHA with IL-4 were seen. 3) TNF induces direct thymocyte apoptosis (a property not shared by IL-1 beta, IL-2, IL-4, IL-6 and IL-7). Of the cytokines studied, only IL-7 reduced TNF apoptosis. Thymocyte apoptosis by TNF showed the same species specificity as costimulation (i.e., human TNF had no effect) and was not inhibited by CY. The thymocyte CD4-CD8 phenotype after 72-h cultures showed that TNF decreased mainly double negative (DN) and single positive (SP) subsets, whereas IL-6 with low or high PHA increased DN and SP, especially the SP CD8+ subset. The regulatory and apoptotic effects of TNF were seen only with thymocytes and not with peripheral splenic or lymph node T cells. Four mAb to mouse TNF (2E2, XT22, **1C6**, and 1OD9) could abrogate TNF costimulation and the TNF effects on IL-6-induced thymocyte proliferation, at both augmenting and inhibitory PHA conditions. However, only the two **antibodies** that also neutralize TNF lytic activity (2E2, XT22) could inhibit TNF-mediated apoptosis, implying two different but neighboring functional domains in the TNF molecule mediating apoptosis/lysis and costimulation. Our studies show that TNF might have unique and complex regulatory effects on growth and death of thymocyte populations in adult mice quite different from its effects on T cells in periphery.

L3 ANSWER 30 OF 55 CAPLUS COPYRIGHT 2003 ACS on STN

1993:577280 Document No. 119:177280 Identification of mRNA-binding proteins of the lower trypanosomatid Leptomonas collosoma. Michaeli, Shulamit; Goldring, Anat; Agabian, Nina (Dep. Membr. Res. Biophys., Weizmann Inst. Sci., Rehovot, 76100, Israel). Experimental Parasitology, 76(3), 308-13 (English) 1993. CODEN: EXPAAA. ISSN: 0014-4894.

AB This report constitutes the first attempt to purify and analyze mRNA-binding proteins from trypanosomatids. Since, as yet, no cis-splicing has been found in these organisms, this system offers an ideal model to study the machinery which is specific for trans-splicing. Using the fractionation methods presented in this study, mRNA binding proteins could be easily obtained in quantities sufficient for generating specific **antibody** reagents to the trypanosomatid proteins. Elucidating the relatedness between these proteins of trypanosomatids and higher eukaryotes may contribute to the understanding of the evolution of RNA maturation, esp. considering the early divergence of trypanosomatids from the eukaryotic lineage. The **1C6** and 5B9 cross-reacting antigens are the first-described mRNA-binding proteins which are conserved throughout great evolutionary distance from trypanosomatids to man.

L3 ANSWER 31 OF 55 MEDLINE on STN DUPLICATE 17

94081027 Document Number: 94081027. PubMed ID: 7505002. A monoclonal **antibody** against human decay-accelerating factor (DAF, CD55), D17, which lacks reactivity with semen-DAF. Hara T; Matsumoto M; Fukumori Y; Miyagawa S; Hatanaka M; Kinoshita T; Seya T; Akedo H. (Department of Immunology, Center for Adult Diseases Osaka, Japan.) IMMUNOLOGY LETTERS, (1993 Aug) 37 (2-3) 145-52. Journal code: 7910006. ISSN: 0165-2478. Pub. country: Netherlands. Language: English.

AB Human decay-accelerating factor (DAF, CD55) is a phosphatidyl inositol-anchored glycoprotein consisting, from the N-terminus, of 4 short

consensus repeats (SCR), a Ser/Thr (ST)-rich region providing O-glycosylation sites, and the membrane-anchoring unit. A mAb, named D17, was raised against purified erythrocyte-DAF. This mAb recognized DAF on blood cells and most cell lines as determined by flow cytometry and immunoblotting. Its reactivity was similar to but weaker than that of two other well-characterized mAbs to DAF, IA10 (seeing an epitope within SCR1) and **1C6** (seeing an epitope within SCR3). The reactivity of D17 with erythrocyte DAF became increased by treatment with sialidase/O-glycanase, suggesting that its epitope is located close to the O-glycosylation sites, probably within the ST-rich region or SCR4. D17 barely blocked the decay-accelerating activity of DAF. Using the three mAbs, tissue-associated and soluble forms of DAF were identified by SDS-PAGE/immunoblotting and immunohistochemical staining. IA10 and **1C6** recognized a 50 kDa protein in spermatozoa lysate and two proteins of Mr 70 and 55 kDa, respectively, in seminal fluid. These represented membrane-associated and soluble forms of DAF, which were neither recognized by mAb against membrane cofactor protein (MCP, CD46) and C3b/C4b receptor (CR1, CD35) nor by non-immune IgG. In contrast to IA10 and **1C6**, D17 did not recognize either spermatozoa-DAF or seminal plasma-DAF, or the deglycosylated or untreated forms of them. Immunohistochemical analysis showed that testis was stained with IA10 but not with D17.(ABSTRACT TRUNCATED AT 250 WORDS)

L3 ANSWER 32 OF 55 MEDLINE on STN DUPLICATE 18

93017904 Document Number: 93017904. PubMed ID: 1383332. Mapping of epitopes, glycosylation sites, and complement regulatory domains in human decay accelerating factor. Coyne K E; Hall S E; Thompson S; Arce M A; Kinoshita T; Fujita T; Anstee D J; Rosse W; Lublin D M. (Department of Pathology, Washington University School of Medicine, St. Louis 63110.) JOURNAL OF IMMUNOLOGY, (1992 Nov 1) 149 (9) 2906-13. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Decay accelerating factor (DAF, CD55) is a glycophospholipid-anchored membrane protein that protects cells from complement-mediated damage by inhibiting the formation and accelerating the decay of C3/C5 convertases. DAF deletion mutants lacking each of the four short consensus repeats (SCR) or the serine/threonine-rich region (S/T) were created by site-directed mutagenesis. These deletion mutants were expressed by stable transfection in Chinese hamster ovary cells for the purpose of mapping important structural and functional sites in DAF. The epitopes on DAF for 16 murine mAb were mapped by immunoprecipitation studies as follows: SCR1, 6; SCR2, 3; SCR3, 3; SCR4, 3; S/T, 1. Testing of 13 mAb showed complete blocking of DAF function only by **1C6** and 1H4, both directed at SCR3. The single N-linked glycosylation site was confirmed at a location between SCR1 and SCR2, and the multiple O-linked oligosaccharides were localized to the S/T region. Functional activity of DAF mutants was assessed by the ability of these transfected constructs to protect Chinese hamster ovary cells from cytotoxicity induced by rabbit **antibody** plus human complement. Removal of SCR1 had no effect on DAF function, but individual deletion of SCR2, SCR3, or SCR4 totally abolished DAF function. Surprisingly, deletion of the S/T region totally abrogated DAF function, but this could be restored by a fusion construct placing the four SCR domains of DAF onto the HLA-B44 molecule, implying that the O-glycosylated S/T region serves as an important but nonspecific spacer projecting the DAF functional domains above the plasma membrane. Overall, the creation of DAF deletion mutants has elucidated important structure-function relations in the DAF molecule.

L3 ANSWER 33 OF 55 MEDLINE on STN DUPLICATE 19

92373022 Document Number: 92373022. PubMed ID: 1380538. Decay-accelerating factor functions as a signal transducing molecule for human monocytes. Shibuya K; Abe T; Fujita T. (Institute of Clinical Medicine, University of Tsukuba, Japan.) JOURNAL OF IMMUNOLOGY, (1992 Sep 1) 149 (5) 1758-62. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Decay-accelerating factor (DAF) is a glycosylphosphatidylinositol-anchored membrane protein that protects cells from damage by autologous complement activation. Of the four mAb against DAF prepared in our laboratory, **1C6** completely blocked DAF function, whereas 5B2 partially blocked it. Using these mAb, we investigated whether human monocytes were activated via DAF molecules. When monocytes were incubated with **1C6** alone, glucose was consumed in significant amounts and phagocytosis of latex beads was enhanced, indicating that the monocytes had been activated. However, **1C6** did not enhance the production of monokines, TNF-alpha, and IL-1 alpha and -beta. The F(ab')2 fragment of **1C6** also activated monocytes, whereas 5B2 and the Fab fragment of **1C6** could not. To further examine monocyte activation, these cells were treated with phosphatidylinositol-specific phospholipase C. Increased glucose consumption and enhanced phagocytic activity by **1C6** were considerably reduced in monocytes treated with phosphatidylinositol-specific phospholipase C. In addition, we found that **1C6** stimulated the generation of inositol trisphosphate. These results demonstrate that the signal transmitted via the DAF molecule is capable of stimulating monocytes.

L3 ANSWER 34 OF 55 MEDLINE on STN DUPLICATE 20

92309134 Document Number: 92309134. PubMed ID: 1377239. Immunological analysis of proteoglycan structural changes in the early stage of experimental osteoarthritic canine cartilage lesions. Pelletier J P; Martel-Pelletier J; Mehraban F; Malemud C J. (University of Montreal, Rheumatic Disease Unit, Notre-Dame Hospital Research Center, Canada.) JOURNAL OF ORTHOPAEDIC RESEARCH, (1992 Jul) 10 (4) 511-23. Journal code: 8404726. ISSN: 0736-0266. Pub. country: United States. Language: English.

AB Specific modifications of the proteoglycan (PG) structure of osteoarthritic (OA) dog cartilage in relation to endogenous metalloprotease activity were examined using murine anti-proteoglycan monoclonal **antibodies** (MoAbs). OA lesions were induced over a period of 8 weeks in crossbred dogs (Pond-Nuki model). The articular cartilage was removed and homogenized in a Tris buffer, pH 7.5, and then divided into four groups: direct PG extraction, no addition, presence of 1 mM p-aminophenyl mercuric acetate (APMA), and presence of 1 mM APMA and 10 mM o-phenanthroline, incubated for 42 h at 37 degrees C followed by PG extraction. MoAbs reactive with PG protein and carbohydrate epitopes included **1C6**, 3B3, 5D4, D1B2, and m4D6. The results showed marked alterations induced by APMA activation of the endogenous metalloproteases. PG changes were apparent at at least three sites: one was either in the hyaluronic acid-binding region or between the hyaluronic-binding region and the G2 globular domain, another was between the keratan-sulfate-rich domain and the chondroitin sulfate-attachment domain, and a third was in the chondroitin sulfate-attachment domain. Constitutive metalloprotease activity resulted in less marked PG alterations with preservation of functional PG aggregation to hyaluronan.

L3 ANSWER 35 OF 55 MEDLINE on STN DUPLICATE 21

93164929 Document Number: 93164929. PubMed ID: 1287411. Synthesis of low buoyant density proteoglycans by human chondrocytes in culture. Malemud C J; Papay R S. (Department of Medicine, Case Western Reserve University, Cleveland, OH 44106.) MATRIX, (1992 Dec) 12 (6) 427-38. Journal code: 8906139. ISSN: 0934-8832. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Human chondrocyte strains were derived from explant outgrowth of nonarthritic or osteoarthritic human cartilage. Chondrocytes radiolabeled with [35SO4] or [35S]-methionine were used to measure the biosynthesis of proteoglycans recovered from the most buoyant fraction (A4) of a CsCl density gradient centrifugation performed under associative conditions. The proteoglycans isolated from the A4 fraction (rho.< 1.47 g/ml) were hydrodynamically small and contained both large and small glycosaminoglycan chains. When assessed by SDS/PAGE using 3-16% gradient gels, two subpopulations of small proteoglycans (smPG) were identified.

The larger of the two species (smPG-I) migrated slower than the 200 kDa marker protein; when reassessed on 3-5% acrylamide gels, its apparent molecular mass was larger than the 480 kDa and 440 kDa alpha and beta heavy chains of dynein. We estimated the apparent molecular size of this smPG to be approximately 520 kDa. The smaller smPG (smPG-II) had an apparent average molecular mass of 180 kDa (range 170-210 kDa) after 3-16% SDS/PAGE. Three monoclonal **antibodies**, **1C6**, 5D4, and S103L, reactive with the hyaluronic acid binding region of the aggregating proteoglycan core protein, keratan sulfate, and a core protein domain in the chondroitin sulfate attachment region, respectively, reacted with a single protein (apparent molecular mass, 180 kDa) that was similar in size to smPG-II.

L3 ANSWER 36 OF 55 MEDLINE on STN DUPLICATE 22

93037466 Document Number: 93037466. PubMed ID: 1384430. Monoclonal **antibodies** directed against epitopes within the core protein structure of the large aggregating proteoglycan (aggrecan) from the swarm rat chondrosarcoma. Calabro A; Hascall V C; Caterson B. (Bone Research Branch, National Institute of Dental Research, National Institutes of Health, Bethesda, Maryland 20892.) ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1992 Nov 1) 298 (2) 349-60. Journal code: 0372430. ISSN: 0003-9861. Pub. country: United States. Language: English.

AB The core protein of the large hyaline cartilage proteoglycan, aggrecan, is composed of six distinct domains: globular 1 (G1), interglobular, globular 2 (G2), keratan sulfate attachment, chondroitin sulfate (CS) attachment, and globular 3 (G3). Monoclonal **antibodies** that recognize epitopes in these domains were raised against Swarm rat chondrosarcoma aggrecan that was either denatured through reduction and alkylation or partially deglycosylated through chondroitinase ABC digestion or alkali elimination, the latter with or without sulfite addition. Monoclonal **antibodies** were further characterized for reactivity to purified aggrecan substructures including rat chondrosarcoma G1 and CS attachment domains, a recombinant rat chondrosarcoma G3 domain fusion protein, bovine articular cartilage G2 domain, and rat chondrosarcoma link protein (LP). Biochemical characterization of the specificities of these monoclonal **antibodies** indicated that one (**1C6**) recognized an epitope shared by both the G1 and the G2 domains; one (5C4) recognized an epitope shared by both LP and the G1 domain; one (7D1) recognized an epitope shared by both the G1 and the CS attachment domains; two (14A1 and 15B2) recognized epitopes in the CS attachment domain; one (14B4) recognized an epitope in the G3 domain; and one (13D1) recognized a ubiquitous epitope shared by the G1, G2, G3, and CS attachment domains of aggrecan and also LP. Collectively the specificities of these **antibodies** confirm the occurrence of multiple repeated epitopes (both carbohydrate and protein in nature) throughout the different domain structures of aggrecan. These **antibodies** have been proven to be useful for identifying aggrecan-like molecules in several connective tissues other than cartilage.

L3 ANSWER 37 OF 55 MEDLINE on STN DUPLICATE 23

92328838 Document Number: 92328838. PubMed ID: 1627172. A small proteoglycan isolated from human cartilage containing a nonfunctional hyaluronic acid binding region. Thomas E; Papay R S; Goldberg V M; Malemud C J. (Department of Medicine, Case Western Reserve University, Cleveland, Ohio 44106.) BIOCHEMISTRY INTERNATIONAL, (1992 Jun) 27 (1) 165-72. Journal code: 8100311. ISSN: 0158-5231. Pub. country: Australia. Language: English.

AB A low buoyant density fraction (A4) was isolated from human cartilage by CsCl density gradient ultracentrifugation. This fraction contained a hydrodynamically small proteoglycan (Kav, 0.74 on Sepharose CL-2B) that reacted with monoclonal **antibody** 12/20/**1C6** specific for the hyaluronic acid binding region (G1 globe) of the large aggregating high-density proteoglycan isolated from many animal cartilages. Despite the presence of the hyaluronic acid binding region, this small

proteoglycan did not form proteoglycan aggregates with hyaluronan, not even in the presence of link protein.

L3 ANSWER 38 OF 55 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 24

92018268 EMBASE Document No.: 1992018268. Presence of human chromosome 1 with expression of human decay-accelerating factor (DAF) prevents lysis of mouse/human hybrid cells by human complement. Wang M.-W.; Wright L.J.; Sims M.J.; White D.J.G.. Department of Animal Physiology, Amylin Corporation, 9373 Towne Centre Drive, San Diego, CA 92121, United States. Scandinavian Journal of Immunology 34/6 (771-778) 1991. ISSN: 0300-9475. CODEN: SJIMAX. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Xenogeneic organs transplanted to phylogenetically distant species are subject to rapid destruction mediated by complement. In humans, the complement activation is regulated by several proteins encoded by a series of closely linked genes (RCA locus) located on chromosome 1. The mouse/human hybrid cell line B10 was found to have retained human chromosome 1. FACS analysis confirmed that RCA products such as decay-accelerating factor (DAF) were expressed on the membrane surface of B10 cells. When exposed to human or rabbit complement in the presence of 'naturally occurring' human anti-mouse **antibodies** these cells were not lysed by human complement but were killed by rabbit complement. This effect could be abrogated by addition of anti-DAF monoclonal **antibody** (**1C6**). The results offer potential for genetic manipulation of the human complement regulatory products in animals to overcome xenograft hyperacute rejection.

L3 ANSWER 39 OF 55 CAPLUS COPYRIGHT 2003 ACS on STN

1991:469760 Document No. 115:69760 Plasma membrane association of primary biliary cirrhosis mitochondrial marker antigen M2. Sundin, Ulf; Sundqvist, K. G. (Karolinska Inst., Huddinge Hosp., Huddinge, S-14186, Swed.). Clinical and Experimental Immunology, 83(3), 407-12 (English) 1991. CODEN: CEXIAL. ISSN: 0009-9104.

AB Decay-accelerating factor (DAF), a membrane inhibitor of homologous complement activation, is present in synovial cells lining joint space and detected in synovial fluid. DAF is considered to protect synovial membrane from complement-mediated injury assocd. with articular inflammation. The immunohistopathol. features of DAF mols. in synovial membrane of rheumatoid synovitis were studied by using a DAF-specific monoclonal **antibody**, **1C6**. Reacting mols. with the **1C6 antibodies** in synovial tissue exts. formed a 70-kD band in Western blot anal. DAF was strongly detected on the flat synovial lining cells, but weakly on the hyperplastic and multi-layered lining cells in rheumatoid synovitis. The latter cells reacted with anti-Leu-M3 **antibodies** specific for a cell surface marker of activated macrophages, sometimes accompanied by C3 and IgM deposition on the superficial synovial membrane. Apparently, active rheumatoid synovitis characteristically with hyperplastic synovial lining cells is out of control by DAF, thereby permitting further complement-mediated injury.

L3 ANSWER 40 OF 55 MEDLINE on STN DUPLICATE 25

91168417 Document Number: 91168417. PubMed ID: 1706235. Expression of decay-accelerating factor is reduced on hyperplastic synovial lining cells in rheumatoid synovitis. Itoh J; Nose M; Fujita T; Kato M; Ohyama A; Kyogoku M. (Department of Pathology, Tohoku University School of Medicine, Sendai, Japan.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 Mar) 83 (3) 364-8. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Decay-accelerating factor (DAF), a membrane inhibitor of homologous complement activation, is present in synovial cells lining joint space and detected in synovial fluid. DAF is considered to protect synovial membrane from complement-mediated injury associated with articular inflammation. We studied the immunohistopathological features of DAF

molecules in synovial membrane of rheumatoid synovitis using a DAF-specific monoclonal **antibody**, **1C6**. Reacting molecules with the **1C6 antibodies** in synovial tissue extracts formed a 70-kD band in Western blot analysis. DAF was strongly detected on the flat synovial lining cells, but weakly on the hyperplastic and multi-layered lining cells in rheumatoid synovitis. The latter cells reacted with anti-Leu-M3 **antibodies** specific for a cell surface marker of activated macrophages, sometimes accompanied by C3 and IgM deposition on the superficial synovial membrane. These results suggest that active rheumatoid synovitis characteristically with hyperplastic synovial lining cells is out of control by DAF, thereby permitting further complement-mediated injury.

L3 ANSWER 41 OF 55 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
91:136267 The Genuine Article (R) Number: FA397. EXPRESSION OF DECAY-ACCELERATING FACTOR IS REDUCED ON HYPERPLASTIC SYNOVIAL LINING CELLS IN RHEUMATOID SYNOVITIS. ITOH J; NOSE M (Reprint); FUJITA T; KATO M; OHYAMA A; KYOGOKU M. TOHOKU UNIV, SCH MED, DEPT PATHOL, 2-1 SEIRYO CHO, AOBA KU, SENDAI, MIYAGI 980, JAPAN; FUKUSHIMA MED SCH, DEPT BIOCHEM, FUKUSHIMA 960, JAPAN; YAMAGATA CITY HOSP, YAMAGATA, JAPAN. CLINICAL AND EXPERIMENTAL IMMUNOLOGY (1991) Vol. 83, No. 3, pp. 364-368. Pub. country: JAPAN. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Decay-accelerating factor (DAF), a membrane inhibitor of homologous complement activation, is present in synovial cells lining joint space and detected in synovial fluid. DAF is considered to protect synovial membrane from complement-mediated injury associated with articular inflammation. We studied the immunohistopathological features of DAF molecules in synovial membrane of rheumatoid synovitis using a DAF-specific monoclonal **antibody**, **1C6**. Reacting molecules with the **1C6 antibodies** in synovial tissue extracts formed a 70-kD band in Western blot analysis. DAF was strongly detected on the flat synovial lining cells, but weakly on the hyperplastic and multi-layered lining cells in rheumatoid synovitis. The latter cells reacted with anti-Leu-M3 **antibodies** specific for a cell surface marker of activated macrophages, sometimes accompanied by C3 and IgM deposition on the superficial synovial membrane. These results suggest that active rheumatoid synovitis characteristically with hyperplastic synovial lining cells is out of control by DAF, thereby permitting further complement-mediated injury.

L3 ANSWER 42 OF 55 MEDLINE on STN DUPLICATE 26
91010805 Document Number: 91010805. PubMed ID: 2120345. Immune responses during human Schistosoma mansoni. XVII. Recognition by monoclonal anti-idiotypic **antibodies** of several idiotopes on a monoclonal anti-soluble schistosomal egg antigen **antibody** and anti-soluble schistosomal egg antigen **antibodies** from patients with different clinical forms of infection. Montesano M A; Freeman G L Jr; Gazzinelli G; Colley D G. (Universidade Federal de Juiz de Fora, MG, Brazil.) JOURNAL OF IMMUNOLOGY, (1990 Nov 1) 145 (9) 3095-9. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB A monoclonal human anti-soluble schistosomal egg Ag(SEA) **antibody** (E5) that stimulates anti-Id T cells and is idiotypically represented in pools of immunoaffinity-purified human anti-SEA **antibodies** from chronic, generally asymptomatic, intestinal (INT) patients (AM1 and AM5) was used to raise several monoclonal anti-Id: 1C2, **1C6**, 4A8, 4F9, and 2A7. Cross-inhibition between these anti-Id identified distinct idiotopes on E5. Anti-SEA preparations from schistosomiasis patients (AM1, AM5, and others) were tested for their inhibition of the E5/monoclonal anti-Id reactions, in competitive ELISA. In either the E5/4A8 or E5/**1C6** ELISA system, anti-SEA from INT (AM1 or AM5) or hepatointestinal (HI) (AM7) patients were able to inhibit these reactions. However, anti-SEA **antibodies** from acute (AM9) or hepatosplenic (HS) (AM3 or AM8) patients did not express Id that were inhibitory in

these systems. These results suggest that a relatively high proportion of INT and HI anti-SEA **antibodies** express a dominant cross-reactive idiotope (CRI) recognized by **1C6**/4A8. This CRI is also easily detected in plasmas from individual INT patients. Anti-Id 1C2 reacted strongly with an Id in AM1, AM5, or AM7, but one which also occurred, to a lesser extent, in AM3, AM8, and AM9. Monoclonal anti-Id 4F9 and 2A7 reacted weakly with idiotopes expressed by **antibodies** from all patients, regardless of the clinical form of their infection. These observations indicate that anti-SEA **antibodies** from INT and HI, but not acute or HS patients express dominant, CRI that are identified by **1C6**, 4A8, or 1C2 and are also expressed on the INT-derived anti-SEA mAb E5.

L3 ANSWER 43 OF 55 EMBASE
on STN DUPLICATE 27
90311519 EMBASE Document No.: 1990311519. Decay-accelerating factor regulates complement-mediated damage in the human atherosclerotic wall. Niculescu F.; Rus H.G.; Vlaicu R.. Medical Clinic No. 1, 3-5 Clinicilor,3400 Cluj-Napoca, Romania. Immunology Letters 26/1 (17-24) 1990. ISSN: 0165-2478. CODEN: IMLED6. Pub. Country: Netherlands. Language: English. Summary Language: English.

AB Decay-accelerating factor (DAF) is an intrinsic membrane inhibitor that regulates the activity of C3 and C5 convertases of the classical and alternative complement pathways. Using two monoclonal **antibodies** , **1C6** and IA10, DAF was localized by immunohistochemistry using streptavidin-biotin-peroxidase complex or silver-intensified immunogold techniques in aortic, iliac and femoral samples obtained at surgery and autopsy from 32 patients. DAF was localized on the cells and in the connective tissue matrix of the arterial wall. Fibrous plaques and intimal thickenings presented larger amounts than fatty streaks, intimae and normal areas. By Western blotting analysis, DAF extracted from the arterial wall had a molecular weight of about 67 kDa. Using a double-labeling technique DAF and C5b-9 complexes were co-localized on nucleated cells and on cell debris. The cells isolated after enzyme digestion of the arterial wall were tested for the protective role of DAF to complement-mediated damage. When DAF of the sensitized cells was blocked by monoclonal **antibodies**, complement-mediated cell lysis was enhanced from 10-15% to 60-70%. The effect of anti-DAF **antibodies** was dose-dependent. DAF blocking in the absence of **antibodies** used for sensitization led to a lysis under 10%. These data suggest a protective role of DAF against autologous complement activation, however insufficient to prevent complement activation in the human atherosclerotic wall.

L3 ANSWER 44 OF 55 BIOSIS on STN
1991:62622 Document No.: PREV199140027977; BR40:27977. ALTERATION IN THE HYALURONIC ACID BINDING REGION HABR EPITOPE RECOGNIZED BY MONOCLONAL **ANTIBODY 1C6** IN HUMAN RHEUMATOID ARTHRITIC RA CARTILAGE PROTEOGLYCAN PG. MALEMUD C J [Reprint author]; PELLETIER J-P; REBERT N; CLOUTIER J-M; MARTEL-PELLETIER J. CWRU, CLEVELAND, OHIO 44106, USA. Arthritis and Rheumatism, (1990) Vol. 33, No. 9 SUPPL, pp. S13. Meeting Info.: 54TH ANNUAL MEETING OF THE AMERICAN COLLEGE OF RHEUMATOLOGY, SEATTLE, WASHINGTON, USA, OCTOBER 27-NOVEMBER 1, 1990. ARTHRITIS RHEUM.
CODEN: ARHEAW. ISSN: 0004-3591. Language: ENGLISH.

L3 ANSWER 45 OF 55 MEDLINE on STN DUPLICATE 28
90063546 Document Number: 90063546. PubMed ID: 2479716. Identification of immunogenic regions of the major coat protein of human papillomavirus type 16 that contain type-restricted epitopes. Cason J; Patel D; Naylor J; Lunney D; Shepherd P S; Best J M; McCance D J. (Richard Dimbleby Laboratory of Cancer Virology, St Thomas' Campus, London, U.K.) JOURNAL OF GENERAL VIROLOGY, (1989 Nov) 70 (Pt 11) 2973-87. Journal code: 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language:

English.

AB We have identified regions of the major capsid protein, L1, of the human papillomavirus (HPV) type 16 (HPV-16 L1), that are recognized by five monoclonal **antibodies** (MAbs) raised to a bacterial fusion protein containing residues 172 to 375 of HPV-16 L1. All five MAbs recognized HPV-16-infected tissue sections by immunohistochemistry, but not sections infected with HPV-1a (cutaneous warts), HPV-6b or -11 (genital warts). MAbs 3D1, 5A4 and 1D6 also recognized HPV-2-infected sections (cutaneous warts); MAb 8C4 recognized only sections containing HPV-16. Four MAbs (8C4, 3D1, 1D6 and 5A4) recognized a synthetic peptide corresponding to residues 269 to 284 of HPV-16 L1; within this region a minimum **antibody** binding site was identified, a tripeptide 276 to 278. However the complete epitope appears to extend beyond these residues and beyond HPV-16 L1 (269 to 284). The fifth MAb, **1C6**, recognized bacterial fusion proteins containing HPV-6b L1, -16 L1 or -18 L1 using immunoblots, yet appeared HPV-16-specific when tested on infected tissue sections. This MAb recognized five amino acids within a different region of HPV-16 L1 (residues 299 to 313).

L3 ANSWER 46 OF 55 MEDLINE on STN DUPLICATE 29

89234179 Document Number: 89234179. PubMed ID: 2469681. Immunoelectron microscopic localization of hyaluronic acid-binding region and link protein epitopes in brain. Ripellino J A; Margolis R U; Margolis R K. (Department of Pharmacology, New York University Medical Center, New York 10016.) JOURNAL OF CELL BIOLOGY, (1989 May) 108 (5) 1899-907. Journal code: 0375356. ISSN: 0021-9525. Pub. country: United States. Language: English.

AB The **1C6** monoclonal **antibody** to the hyaluronic acid-binding region weakly stained a 65-kD component in immunoblots of the chondroitin sulfate proteoglycans of brain, and the 8A4 monoclonal **antibody**, which recognizes two epitopes in the polypeptide portion of link protein, produced strong staining of a 45-kD component present in the brain proteoglycans. These **antibodies** were utilized to examine the localization of hyaluronic acid-binding region and link protein epitopes in rat cerebellum. Like the chondroitin sulfate proteoglycans themselves and hyaluronic acid, hyaluronic acid-binding region and link protein immunoreactivity changed from a predominantly extracellular to an intracellular (cytoplasmic and intra-axonal) location during the first postnatal month of brain development. The cell types which showed staining of hyaluronic acid-binding region and link protein, such as granule cells and their axons (the parallel fibers), astrocytes, and certain myelinated fibers, were generally the same as those previously found to contain chondroitin sulfate proteoglycans and hyaluronic acid. Prominent staining of some cell nuclei was also observed. In agreement with earlier conclusions concerning the localization of hyaluronic acid and chondroitin sulfate proteoglycans, there was no intracellular staining of Purkinje cells or nerve endings or staining of certain other structures, such as oligodendroglia and synaptic vesicles. The similar localizations and coordinate developmental changes of chondroitin sulfate proteoglycans, hyaluronic acid, hyaluronic acid-binding region, and link protein add further support to previous evidence for the unusual cytoplasmic localization of these proteoglycans in mature brain. Our results also suggest that much of the chondroitin sulfate proteoglycan of brain may exist in the form of aggregates with hyaluronic acid.

L3 ANSWER 47 OF 55 MEDLINE on STN DUPLICATE 30

89341426 Document Number: 89341426. PubMed ID: 2760466. Generation of a sheep x mouse heterohybridoma cell line (**1C6**.3a6T.1D7) and evaluation of its use in the production of ovine monoclonal **antibodies**. Flynn J N; Harkiss G D; Hopkins J. (Department of Veterinary Pathology, University of Edinburgh, Summerhall, U.K.) JOURNAL OF IMMUNOLOGICAL METHODS, (1989 Jul 26) 121 (2) 237-46. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB A stable aminopterin-sensitive sheep X mouse heterohybridoma cell line (

1C6.3a6T.1D7) for use in the generation of sheep monoclonal **antibodies** is described. The line was first constructed by fusing the mouse myeloma line, NSO, to normal sheep lymphocytes obtained from the efferent lymphatic vessel of a cannulated popliteal lymph node. The line was rendered sensitive to aminopterin through a combination of irradiation and treatment with the anti-metabolite drug 6-thioguanine. Characterisation of the cloned cell line showed that it did not secrete sheep immunoglobulin (Ig) molecules, express Ig on the surface membrane, or express normal sheep B or T cell surface markers. The **1C6** .3a6T.1D7 line has remained stable in tissue culture for over 2 years, showing no signs of reversion to aminopterin resistance. The **1C6** .3a6T.1D7 cells have been used as fusion partners with lymphocytes from antigen primed sheep to generate sheep monoclonal **antibodies** to human chorionic gonadotropin (hCG) or a synthetic peptide analogue of the VP1 capsid protein of foot and mouth disease virus (FMDV). To optimise the efficiency of heterohybridoma generation, comparisons were made of peripheral blood, efferent lymph or excised lymph nodes as sources of antigen-stimulated lymphocytes for fusion. The results showed that lymphocytes prepared from either efferent lymph or lymph node on the fourth day following antigenic stimulation gave similar high fusion efficiencies, and both were vastly superior to peripheral blood lymphocytes. Results were also obtained which showed that the blast cells present in lymphoid tissues due to antigenic stimulation were the major cell types involved in the generation of viable **antibody** -secreting sheep X sheep X mouse heterohybridomas.

L3 ANSWER 48 OF 55 MEDLINE on STN DUPLICATE 31

90319768 Document Number: 90319768. PubMed ID: 2561751. Detection of cytomegalovirus in paraffin-embedded lung tissue sections. Honda Y. SCIENCE REPORTS OF THE RESEARCH INSTITUTE, TOHOKU UNIVERSITY. SER. C: MEDICINE, (1989 Dec) 36 (1-4) 17-28. Journal code: 0234153. ISSN: 0371-2761. Pub. country: Japan. Language: English.

AB Attempts were made to detect cytomegalovirus (CMV) in paraffin-embedded lung tissue sections from five patients with malignant disease by the immunofluorescence and immunoperoxidase methods with application of monoclonal **antibodies** against CMV and by localization of DNA by the method of in situ hybridization using a biotinylated probe. In the immunofluorescence method, the monoclonal **antibody 1C6** stained a large number of CMV-infected cells. However, nonspecific staining of the bronchoepithelial cells was a disadvantage of this method. In the immunoperoxidase staining, the monoclonal **antibodies** E. 13 and CCH2 gave highly sensitive and specific results. These monoclonal **antibodies** stained the nuclei of the infected cells even in the absence of viral inclusions. In the viral DNA probe technique, three specimens were found to contain hybridizing cells. The DNA probe detected not only cytopathic cells but also normal-appearing infected cells. The number of cells stained by the DNA probe was much smaller than that stained by the immunoperoxidase method. The author concludes that the immunoperoxidase technique using monoclonal **antibodies** against CMV is useful for the diagnosis of CMV infection in the paraffin-embedded lung tissue. Localization of DNA by the method of in situ hybridization is not as useful as the immunoperoxidase method because of lower sensitivity.

L3 ANSWER 49 OF 55 CAPLUS COPYRIGHT 2003 ACS on STN

1995:961137 Document No. 124:3269 Isolation and characterization of peptides bearing the epitope for monoclonal **antibody** 1-c-6 from swarm rat chondrosarcoma proteoglycan. Hejna, Michael John (College of Nursing, Rush Univ., Chicago, IL, USA). 159 pp. Avail. Univ. Microfilms Int., Order No. DA9530341 From: Diss. Abstr. Int., B 1995, 56(5), 2608 (English) 1988.

AB Unavailable

L3 ANSWER 50 OF 55 MEDLINE on STN DUPLICATE 32

88314135 Document Number: 88314135. PubMed ID: 2457546. Purification and characterization of decay-accelerating factor (DAF) from Raji cells. Fujita T; Shinkai Y; Inoue T; Tamura N. (Department of Immunology, University of Tsukuba, Ibaraki-ken, Japan.) IMMUNOLOGY, (1988 Jul) 64 (3) 369-74. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Decay-accelerating factor (DAF), a membrane protein that regulates the complement system, was purified to homogeneity from lymphoblastoid (Raji) cells (DAF-R). It exhibited almost the same molecular weight as DAF from stroma of erythrocytes (DAF-S). Purified DAF-R, which could be reincorporated into cell membranes, accelerated the decay of the C3 convertases, in both the classical (C4b2a) and the alternative (C3bBb) pathways. This activity was completely inhibited by a monoclonal anti-DAF **antibody**, **1C6**. From these results, DAF-R and DAF-S can not be distinguished; however, the decay-accelerating activity of DAF-R was much higher than that of DAF-S. **1C6** enhanced the binding of C3 to Raji cells by incubating with six purified components of the alternative pathway, whereas it did not induce the killing of Raji cells after a short incubation period. When **antibodies** against Raji cells were added to the above system, the blocking of DAF activity by **1C6** resulted in efficient killing of Raji cells by autologous complement. From these results, it is clear that DAF on nucleated cells plays an important role in protecting these cells from the damage caused by autologous complement.

L3 ANSWER 51 OF 55 MEDLINE on STN DUPLICATE 33

88029256 Document Number: 88029256. PubMed ID: 2822376. The heterogeneity of isolated adult rat Leydig cells separated on Percoll density gradients: an immunological, cytochemical, and functional analysis. Hedger M P; Eddy E M. (Gamete Biology Section, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina 27709.) ENDOCRINOLOGY, (1987 Nov) 121 (5) 1824-38. Journal code: 0375040. ISSN: 0013-7227. Pub. country: United States. Language: English.

AB Intertubular cells, isolated from adult rat testes by collagenase dispersal under conditions designed to minimize cell damage, were fractionated on Percoll density gradients. In the gradient fractions, there was a close cellular correlation between the presence of 3 beta-hydroxysteroid dehydrogenase (3 beta HSD), determined by cytochemistry, and other Leydig cell markers (nonspecific esterase, autofluorescence, and an antigen defined by monoclonal **antibody** LC-**1C6**). As the reagents for 3 beta HSD cytochemistry are excluded by intact membranes, Leydig cells with damaged plasma membranes were identified by 3 beta HSD reactivity in suspended cell preparations, and the total number of 3 beta HSD-positive (3 beta HSD+) cells in the same preparations was determined after lysis of the cell membrane. Whole cells were differentiated from cytoplasmic fragments by counterstaining with the nuclear dye propidium iodide, and the number of intact Leydig cells in each preparation was determined subsequently by subtracting the number of damaged nucleated 3 beta HSD+ cells from the total number of nucleated 3 beta HSD+ cells. The majority of intact isolated Leydig cells were found in gradient fractions of 1.054-1.096 g/ml density. Acute (3-H) basal and hCG-stimulated testosterone production per intact Leydig cell were dependent upon the concentration of Leydig cells per assay well, indicating that there is cooperativity among Leydig cells in vitro. There was no difference in steroidogenic function among intact Leydig cells from different fractions of the above density gradient range at assay concentrations greater than 10,000 Leydig cells/well. At lower cell concentrations, Leydig cells from gradient fractions of lower density (1.054-1.064 g/ml) produced slightly less testosterone in response to hCG stimulation than Leydig cells from more dense fractions (1.070-1.096 g/ml). Prolonging the exposure of isolated cells to the dispersal conditions caused declines in the apparent buoyant density and basal testosterone and hCG-stimulated cAMP and testosterone production of all Leydig cells, without detectable changes in cell integrity. The data

indicate that both the absolute steroidogenic function and the functional heterogeneity of isolated intact Leydig cells are, at least in part, dependent upon the procedures used for their isolation.

L3 ANSWER 52 OF 55 MEDLINE on STN DUPLICATE 34

87151150 Document Number: 87151150. PubMed ID: 2435060. Epitopes on foot-and-mouth disease virus particles. I. Topology. McCullough K C; Crowther J R; Carpenter W C; Brocchi E; Capucci L; De Simone F; Xie Q; McCahon D. VIROLOGY, (1987 Apr) 157 (2) 516-25. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB Monoclonal **antibodies** (MAb) against an O1 Suisse isolate of FMDV were used to identify epitopes on the virus particle and to determine their relative function. Six major antigenic sites containing one or more epitopes were identified using competition ELISA. An epitope relationship is proposed consisting of a trypsin-sensitive sequential site, termed B2/D9, from the codings for the MAb which reacted with it, which was associated with virus infectivity and is probably at or near to the cell-binding site of the virion; a trypsin-resistant, conformational site **1C6**/4C9 MAb reaction at which also resulted in neutralization of virus infectivity; a second trypsin-resistant, conformational site 3C8, where again MAb reaction neutralised virus infectivity; a third trypsin-resistant, conformational site 6C3/2G5, at which MAb-dependent neutralisation of virus infectivity was inefficient; a site 3G4, the expression of which was impaired but not destroyed by trypsin treatment, and was not related to virus infectivity; an internal site A8, which appears to be a "12S subunit-specific" site. This work clearly demonstrates for the first time that both trypsin-sensitive and trypsin-resistant neutralisable (infectivity-associated) sites exist on the FMDV particle, and only one of these can be related to the sequential site used to formulate current FMDV peptide vaccines.

L3 ANSWER 53 OF 55 MEDLINE on STN DUPLICATE 35

87112914 Document Number: 87112914. PubMed ID: 2433462. Functional and antigenic domains of the matrix (M1) protein of influenza A virus. Ye Z P; Pal R; Fox J W; Wagner R R. JOURNAL OF VIROLOGY, (1987 Feb) 61 (2) 239-46. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The membrane- and ribonucleocapsid (RNP)-binding domains of the matrix (M1) protein of influenza A virus (WSN strain) were partially mapped and characterized by reactivity with monoclonal **antibodies** (MAb) as well as by proteolytic cleavages and amino acid sequencing of the resulting peptides. Of two peptides formed by formic acid hydrolysis, a 9-kilodalton fragment at the amino-terminal third of the M1 protein was recognized by MAb M2-**1C6** (to epitope 1), and a 15-kilodalton fragment at the carboxy-terminal two-thirds was recognized by MAb 289/4 (to epitope 2). Partial cleavage by staphylococcal V8 protease gave rise to a 16-kilodalton peptide, mapping to amino acid 8, which was recognized by MAbs to all three epitopes but rather weakly by MAb 904/6 to epitope 3. These studies suggest that epitope 1 of the M1 protein resides between amino acids 8 and 89, whereas epitopes 2 and possibly 3 are located between amino acids 89 and 141 or somewhat more carboxy distal. The intact M1 protein and its N-terminal 9- and 10-kilodalton peptides generated by formic acid or V8 protease cleavage, respectively, reconstituted with dipalmitoylphosphatidylcholine vesicles, but these N-terminal peptides had little effect on in vitro transcription of the RNP core. In sharp contrast, both intact M1 protein and the C-terminal 15-kilodalton formic acid fragment were able to inhibit viral transcription markedly. Moreover, MAb 289/4 (to epitope 2) reversed this inhibited transcription significantly. These studies suggest that the lipid-binding domain of the M1 protein is located within the amino-terminal third, whereas the site involved in the interaction of the M1 protein with RNP cores is located within the carboxy-terminal two-thirds.

L3 ANSWER 54 OF 55 MEDLINE on STN DUPLICATE 36
87157909 Document Number: 87157909. PubMed ID: 3548835. Monoclonal **antibodies** against rat Leydig cell surface antigens. Hedger M P; Eddy E M. BIOLOGY OF REPRODUCTION, (1986 Dec) 35 (5) 1309-19. Journal code: 0207224. ISSN: 0006-3363. Pub. country: United States. Language: English.

AB Monoclonal **antibodies** (MAbs) directed against the Leydig cell surface may be used to identify this cell in testicular preparations. Collagenase-dispersed adult rat interstitial cells were fractionated on Percoll density gradients, and Leydig cell-enriched fractions were used to prepare MAbs. Hybridomas were screened by enzyme-linked immunosorbent assay (ELISA), indirect immunofluorescence assay (IIF) on isolated testicular cells and immunocytochemical localization on paraffin sections of adult testes. In density gradient fractions, immunoglobulin (Ig) M MAbs (LC-**1C6** and LC-6H6) labeled the surface of cells possessing the morphological characteristics of Leydig cells. The density gradient profiles of MAb-binding activity observed by IIF and ELISA were parallel with the Leydig cell distribution as determined by [125I]-human chorionic gonadotropin (hCG) binding, testosterone response to hCG in vitro, 3 beta-hydroxysteroid dehydrogenase histochemistry and electron microscopy. The MAbs prominently labeled most interstitial cells in sections, but there was little or no labeling of connective tissue, endothelial or seminiferous tubule cells. Both MAbs recognized components of Mr 58,000 in Western blots of Leydig cell-enriched extracts. The results indicate that LC-**1C6** and LC-6H6 recognize antigens on the Leydig cell surface that are not present on other isolated testicular cells from the adult rat. These MAbs are specific markers of the Leydig cell in situ and in vitro.

L3 ANSWER 55 OF 55 MEDLINE on STN DUPLICATE 37
86276673 Document Number: 86276673. PubMed ID: 3015780. Immune protection against foot-and-mouth disease virus studied using virus-neutralizing and non-neutralizing concentrations of monoclonal **antibodies**. McCullough K C; Crowther J R; Butcher R N; Carpenter W C; Brocchi E; Capucci L; De Simone F. IMMUNOLOGY, (1986 Jul) 58 (3) 421-8. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Monoclonal **antibodies** (MAb) against sequential or conformational epitopes on foot-and-mouth disease virus (FMDV) passively protected neonatal syngeneic (BALB/c) mice at dilutions at which they could not neutralize virus infectivity in vitro. The B2, D9, **1C6** and 4C9 MAb, against the Group 1 (sequential) and Group 2 (conformational) epitopes, protected the mice at an **antibody**:virion molar ratio of between 38:1 and 84:1 (12-18 times lower than that required for neutralization of virus infectivity in vitro). The 3C8 (Group 3) and 6C3 (Group 4) MAb were, respectively, between 5 and 12 times, and between 18 and 40 times, less efficient at protection. There was no consistent correlation between the efficiency of neutralization of virus infectivity in vitro and the protection of neonatal mice against the virus pathogen. Thus, immune protection against FMDV must use mechanisms other than the direct neutralization of virus infectivity by **antibody**. Complement did not increase the virus neutralization titre of the MAb, but pepsin digestion of the MAb abrogated the enhanced in vivo protection over in vitro neutralization, with little effect on their capacity to neutralize virus infectivity. It is therefore likely that opsonization to a minimum affinity, and subsequent rapid phagocytosis, play a major role in the immune defence against FMDV. This is discussed in terms of the natural host for FMDV and the induction of immunological protection.

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L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
2002:964996 Document No. 138:33697 Endocrine gland-derived vascular endothelial growth factor nucleic acids and polypeptides and their biological activities and use in drug screening and therapies. Ferrara, Napoleone; Watanabe, Colin; Wood, William I.; Shek, Theresa (USA). U.S. Pat. Appl. Publ. US 2002192634 A1 20021219, 105 pp., Cont.-in-part of U.S. Ser. No. 886,242. (English). CODEN: USXXCO. APPLICATION: US 2001-27603 20011219. PRIORITY: US 1998-PV96146 19980811; WO 1999-US12252 19990602; US 1999-PV145698 19990726; US 1999-380137 19990825; WO 2000-US219 20000105; WO 2000-US4914 20000224; WO 2000-US8439 20000330; US 2000-PV213637 20000623; US 2000-PV230978 20000907; US 2000-709238 20001108; WO 2000-US32678 20001201; US 2001-886242 20010620.
AB The present invention is based on the identification and characterization of a novel, tissue-restricted, growth and differentiation factor that acts selectively on one endothelial cell type. This factor, referred to as endocrine gland-derived vascular endothelial growth factor (EG-**VEGF**), induces proliferation, migration, and fenestrations in capillary endothelial cells derived from endocrine glands, but has no effect on a variety of other endothelial and non-endothelial cell types tested. EG-**VEGF** also induces phosphorylation of kinases involved in cell proliferation or survival, including ERK1, ERK2, Akt, and eNOS. EG-**VEGF** nucleic acids and polypeptides can be used in a no. of assays and in diagnosis and treatment of conditions assocd. with hormone-producing tissue. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, **antibodies** which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Also provided herein are methods of screening for modulators of EG-**VEGF**. Furthermore, methods and related methods of treatment are described herein which pertain to regulating cellular proliferation and chemotaxis.

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L8 ANSWER 1 OF 68 CAPLUS COPYRIGHT 2003 ACS on STN
2003:777252 Document No. 139:272097 Protein and cDNA sequences of osteoclast-specific genes from human and mouse, and therapeutic use. Choi, Yongwon (USA). U.S. Pat. Appl. Publ. US 2003186297 A1 20031002, 26 pp. (English). CODEN: USXXCO. APPLICATION: US 2003-368087 20030214. PRIORITY: US 2002-PV368638 20020328.
AB The invention provides protein and cDNA sequences of osteoclast-specific genes, OCL-**2A3**, OCL-1E7, and OCL-5G10, from human and mouse. Methods for using these osteoclast-specific genes and proteins in the detection and isolation of osteoclasts, in prodn. of **antibodies** specific to osteoclasts and to identify agents capable of modulating osteoclast function and treating diseases linked to osteoclasts are also provided.

L8 ANSWER 2 OF 68 CAPLUS COPYRIGHT 2003 ACS on STN
2003:435068 Document No. 139:17564 Modulation of angiogenesis and endothelialization by human laminin complex and **antibody** for antitumor therapy. Jones, Jonathan C. R.; Gonzales, Meredith (USA). U.S. Pat. Appl. Publ. US 2003103975 A1 20030605, 52 pp., Cont.-in-part of U.S. Ser. No. 706,235. (English). CODEN: USXXCO. APPLICATION: US 2002-299058

20021118. PRIORITY: US 1999-PV163199 19991103; US 2000-706235 20001103.
AB A novel laminin complex is described composed of subunits of .alpha.4, .beta.3, and .gamma.1 laminins. Further described is a fragment of .alpha.4 laminin which binds integrin, and agents capable of modulating the binding of .alpha.4 laminin to the .alpha.v.beta.3 integrin receptor. Therapeutic methods are disclosed for inhibiting tumor growth by inhibiting neovascularization. The invention also provides **antibody 2A3** capable of modulating angiogenesis by modulating the binding of .alpha.4 laminin to the integrin. The invention provides protein sequence of human laminin .alpha.4-subunit sequence.

L8 ANSWER 3 OF 68 MEDLINE on STN DUPLICATE 1
2003488564. PubMed ID: 14565771. Preferential metabolic activation of N-nitrosopiperidine as compared to its structural homologue N-nitrosopyrrolidine by rat nasal mucosal microsomes. Wong Hansen L; Murphy Sharon E; Hecht Stephen S. (University of Minnesota Cancer Center, Minneapolis, Minnesota 55455, USA.) Chemical research in toxicology, (2003 Oct) 16 (10) 1298-305. Journal code: 8807448. ISSN: 0893-228X. Pub. country: United States. Language: English.
AB N-Nitrosopiperidine (NPIP) is a potent rat nasal carcinogen whereas N-nitrosopyrrolidine (NPYR), a hepatic carcinogen, is weakly carcinogenic in the nose. NPIP and NPYR may be causative agents in human cancer. P450-catalyzed alpha-hydroxylation is the key activation pathway by which these nitrosamines elicit their carcinogenic effects. We hypothesize that the differences in NPIP and NPYR metabolic activation in the nasal cavity contribute to their differing carcinogenic activities. In this study, the kinetics of tritium-labeled NPIP or NPYR alpha-hydroxylation mediated by Sprague-Dawley rat nasal olfactory or respiratory microsomes were investigated. To compare alpha-hydroxylation rates of the two nitrosamines, tritiated 2-hydroxytetrahydro-2H-pyran and 2-hydroxy-5-methyltetrahydrofuran, the major NPIP alpha-hydroxylation products, and tritiated 2-hydroxytetrahydrofuran, the major NPYR alpha-hydroxylation product, were quantitated by HPLC with UV absorbance and radioflow detection. These microsomes catalyzed the alpha-hydroxylation of NPIP more efficiently than that of NPYR. K(M) values for NPIP were lower as compared to those for NPYR (13.9-34.7 vs 484-7660 muM). Furthermore, catalytic efficiencies (V(max)/K(M)) of NPIP were 20-37-fold higher than those of NPYR. Previous studies showed that P450 **2A3**, present in the rat nose, also exhibited this difference in catalytic efficiency. For both types of nasal microsomes, coumarin (100 muM), a P450 2A inhibitor, inhibited NPIP and NPYR alpha-hydroxylation from 63.8 to 98.5%. Furthermore, **antibodies** toward P450 2A6 inhibited nitrosamine alpha-hydroxylation in these microsomes from 68.8 to 78.4% whereas **antibodies** toward P450 2E1 did not inhibit these reactions. Further immunoinhibition studies suggest some role for P450 2G1 in NPIP metabolism by olfactory microsomes. In conclusion, olfactory and respiratory microsomes from rat nasal mucosa preferentially activate NPIP over NPYR with P450 **2A3** likely playing a key role. These results are consistent with local metabolic activation of nitrosamines as a contributing factor in their tissue-specific carcinogenicity.

L8 ANSWER 4 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 2
2003390429 EMBASE Influences of McAb against S. flexneri-2a on HeLa cell invasion. Wang L.; Gao J.-Y.; Peng H.; Wang H.; Yi S.-Q.. J.-Y. Gao, Inst. of Microbiol. and Epidemiology, Beijing 100071, China. gaojy@nic.bmi.ac.cn. Chinese Journal of Microbiology and Immunology 23/8 (633-635) 30 Aug 2003.
Refs: 3.
ISSN: 0254-5101. CODEN: ZWMZDP. Pub. Country: China. Language: Chinese. Summary Language: English; Chinese.
AB Objective: To identify the effects of MeAbs against membrane protein or LPS of S. flexneri-2a on invading HeLa cells by Shigella flexneri.

Methods: After treated with MeAbs against various membrane antigens, Shigella invaded the HeLa cells. The invasion results were analyzed by microscopy and laser scanning confocal microscopy. Results: MeAb 17G2, 3A6, 1G8 and **2A3** failed to block the course of invasion while increased the number of S. flexneri-2a in HeLa cells. Conclusion: The epitopes identified by these McAbs are associated with the invasion process, which may be a component of protein secretion system.

L8 ANSWER 5 OF 68 CAPLUS COPYRIGHT 2003 ACS on STN
2002:964996 Document No. 138:33697 Endocrine gland-derived vascular endothelial growth factor nucleic acids and polypeptides and their biological activities and use in drug screening and therapies. Ferrara, Napoleone; Watanabe, Colin; Wood, William I.; Shek, Theresa (USA). U.S. Pat. Appl. Publ. US 2002192634 A1 20021219, 105 pp., Cont.-in-part of U.S. Ser. No. 886,242. (English). CODEN: USXXCO. APPLICATION: US 2001-27603 20011219. PRIORITY: US 1998-PV96146 19980811; WO 1999-US12252 19990602; US 1999-PV145698 19990726; US 1999-380137 19990825; WO 2000-US219 20000105; WO 2000-US4914 20000224; WO 2000-US8439 20000330; US 2000-PV213637 20000623; US 2000-PV230978 20000907; US 2000-709238 20001108; WO 2000-US32678 20001201; US 2001-886242 20010620.
AB The present invention is based on the identification and characterization of a novel, tissue-restricted, growth and differentiation factor that acts selectively on one endothelial cell type. This factor, referred to as endocrine gland-derived vascular endothelial growth factor (EG-VEGF), induces proliferation, migration, and fenestrations in capillary endothelial cells derived from endocrine glands, but has no effect on a variety of other endothelial and non-endothelial cell types tested. EG-VEGF also induces phosphorylation of kinases involved in cell proliferation or survival, including ERK1, ERK2, Akt, and eNOS. EG-VEGF nucleic acids and polypeptides can be used in a no. of assays and in diagnosis and treatment of conditions assocd. with hormone-producing tissue. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, **antibodies** which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Also provided herein are methods of screening for modulators of EG-VEGF. Furthermore, methods and related methods of treatment are described herein which pertain to regulating cellular proliferation and chemotaxis.

L8 ANSWER 6 OF 68 CAPLUS COPYRIGHT 2003 ACS on STN
2003:205687 Document No. 138:220029 Effect of Coxsackie B3 virus monoclonal **antibodies** on the appearance of cardiac myocytes and enzyme metabolism. Zhu, Desheng; Li, Hua; Xiang, Rune; Xie, Xiaoming (Center of Experimental Animal, Fourth Military Medical University, Xian, Shanxi Province, 710033, Peop. Rep. China). Disi Junyi Daxue Xuebao, 23(3), 246-249 (Chinese) 2002. CODEN: DJDXEG. ISSN: 1000-2790. Publisher: Disi Junyi Daxue Xuebao Bianjibu.
AB The effect of Coxsackie B3 virus monoclonal **antibodies** on pathogenesis of viral myocarditis was explored by observing the alterations of the appearance of cardiac myocytes and enzymes in culture. The authors prepd. 26 clones of anti-Coxsackie B3 monoclonal **antibodies** (CVB3-mAb). Two clones (**2A3**, 2G12) which combined with rat cardiac myocytes were chosen to interact with beating rat cardiac myocytes cultured in vitro. The myocardial enzyme levels, beating percentage, and cytopathic effect in the culture of monoclonal **antibodies** and rat cardiac myocytes were studied. Twelve clones of viral **antibodies** combined with the myofibrils of rat cardiac myocytes while other 14 clones did not. The selected 2 clones of CVB3-mAb were added to the cultures of beating rat cardiac myocytes and the cultures were examd. at different times. Compared with the controls, myocardial enzyme levels (CK, CK-MB, LDH, LDH-1, HBDH) and troponin (cTn) values of the cultures all increased, and the changes of the appearance of

rat cardiac myocytes were also obsd. Thus, some viral **antibodies** may cause the change in appearance of cardiac myocytes and enzymes in the cultures, which may be the important cause of progressing damage of cardiac myocytes.

L8 ANSWER 7 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
2003:325599 Document No.: PREV200300325599. DEVELOPMENT OF AN ELISA ASSAY TO MEASURE Abeta40 AND Abeta42 IN MOUSE AND RAT BRAIN. Watson, M. D. [Reprint Author]; Perez, S. M. [Reprint Author]; Levine, H. X. [Reprint Author]; Mehta, P.; Emmerling, M. R. [Reprint Author]. Global Res Dev, Pfizer, Ann Arbor, MI, USA. Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 688.4.
http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
Language: English.

AB Animal models are desirable for the development of compounds that reduce cerebral beta-amyloid production. However, it is difficult to measure Abeta in wild type mouse brains due to very low levels of Abeta40 and Abeta42. In addition, a difference of 3 amino acids in the mouse Abeta sequence prohibits the use of existing, highly sensitive human Abeta ELISAs. To measure brain levels of Abeta in mice, we developed an effective amyloid extraction procedure and a sensitive rodent Abeta ELISA. These methods were used to measure Abeta in mice and rats of various ages. Several extraction procedures were tested, of which SDS/DEA extraction was found to be the best. For detection of rodent Abeta40 and Abeta42, **antibody** 4G8 is used for antigen capture, and polyclonal rabbit **antibodies** R209 and R226 for detection of Abeta40 and Abeta42 respectively. In addition, we use a monoclonal **antibody** (**2A3**) to rodent Abeta 1-16 to capture, and 4G8 to detect, total Abeta (which may include C-truncated species). We find that Abeta40 and Abeta42 can be consistently detected in brain extracts of mice and rats. These results support the use of wildtype mice for the study of compounds affecting Abeta production.

L8 ANSWER 8 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 3
2001406565 EMBASE Rat oesophageal cytochrome P450 (CYP) monooxygenase system: Comparison to the liver and relevance in N-nitrosodiethylamine carcinogenesis. Pinto L.F.R.; Moraes E.; Albano R.M.; Silva M.C.; Godoy W.; Glisovic T.; Lang M.A.. L.F.R. Pinto, Departamento de Bioquimica, IBRAG, Universidade do Estado Rio Janeiro, Av. 28 de Setembro 87 fundos 4 andar, Rio de Janeiro, RJ, Brazil. fpinto@uerj.br. Carcinogenesis 22/11 (1877-1883) 2001.
Refs: 48.
ISSN: 0143-3334. CODEN: CRNGDP. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB N-nitrosodiethylamine (NDEA) is able to induce tumours in the rat oesophagus. It has been suggested that this could be due to tissue specific expression of NDEA activating cytochrome P450 enzymes. We investigated this by characterizing the oesophageal monooxygenase complex of male Wistar rats and comparing it with that of the liver. Total amount of cytochrome P450, NADPH P450 reductase, cytochrome b5 and cytochrome b5 reductase of the oesophageal mucosa was .apprx.7% of what was found in the liver. In addition, major differences were found in the cytochrome P450 isoenzyme composition between these organs: CYP 2B1/2B2 and CYP3A were found only in the liver, whereas CYP1A1 was constitutively expressed only in the oesophagus. Of the two well-known nitrosamine metabolizing enzymes, CYP2A3 was found only in the oesophagus whereas CYP2E1 was exclusively expressed in the liver. Catalytic studies, western blotting and RTPCR analyses confirmed the expression of CYP2A3 in the oesophagus. CYP2A enzymes are known to be good catalysts of NDEA metabolism. Oesophageal microsomes had a K(m) for NDEA metabolism, which was about one-third of that of hepatic microsomes, but they showed similar activities when

compared per nmol of total P450. NDEA activity in the oesophagus was significantly increased by coumarin (CO), which also induced oesophageal CYP2A3. Immunoinhibition of the microsomal NDEA activity showed that up to 70% of this reaction is catalysed by CYP2A3 in the oesophagus, whereas no inhibition of the hepatic NDEA activity could be achieved by the anti-CYP2A5 **antibody**. NDEA, but not N-nitrosodimethylamine (NDMA) inhibited the oesophageal metabolism of CO. The results of the present investigation show major differences in the enzyme composition of the oesophageal and hepatic monooxygenase complexes, and are in accordance with the hypothesis that the NDEA organotropism could, to a large extent, be due to the tissue specific expression of the activating enzymes.

L8 ANSWER 9 OF 68 MEDLINE on STN DUPLICATE 4

2001285449 Document Number: 21101893. PubMed ID: 11173525. A single-chain Fv fragment **2A3** specific for native lysozyme: isolation from a human synthetic phage display **antibody** library and characterization. Kikuchi M; Takeda C; Tsujimoto Y; Asada S; Nagata K. (Department of Bioscience & Technology, Faculty of Science & Engineering, Ritsumeikan University, Noji-higashi, Kusatsu, Shiga 525-8577, Japan.. kikuchi@se.ritsumei.ac.jp) . JOURNAL OF BIOCHEMISTRY, (2001 Feb) 129 (2) 237-42. Journal code: 0376600. ISSN: 0021-924X. Pub. country: Japan. Language: English.

AB We have isolated from a human synthetic phage display library a clone, **2A3**, which discriminates native lysozyme from denatured forms. Binding of single-chain Fv fragments (scFvs) of the clone to native hen egg white lysozyme was competitively inhibited by native hen egg white (hew) and human (h) lysozymes. Dot blotting analysis indicated that scFv of the clone did not react with denatured lysozymes. The K(d) values for scFv of **2A3** binding to native hew- and h-lysozymes were 3.78 x 10(-9) and 9.31 x 10(-9) M, respectively, indicating that **2A3** binds more strongly to native hew-lysozyme than to native h-lysozyme. The deduced amino acid sequence of the V(H) chain-CDR3 region of **2A3** was RRYALDY, of which the Arg residues at positions 1 and 2 of the CDR3 region were observed to be extremely rare in other **antibodies** by homology analysis. Based on these observations, site-directed mutagenesis of the RRYALDY-coding region was carried out. The results, combined with biomolecular analyses, demonstrated that Arg residues at positions 1 and 2 of this region were important for native lysozyme-binding.

L8 ANSWER 10 OF 68 CAPLUS COPYRIGHT 2003 ACS on STN

2001:131868 Document No. 135:208790 Expression and properties of Rab25 in polarized Madin-Darby canine kidney cells. Goldenring, James R.; Aron, Lorraine M.; Lapierre, Lynne A.; Navarre, Jennifer; Casanova, James E. (Institute for Molecular Medicine and Genetics, Departments of Medicine, Surgery, Cellular Biology and Anatomy, Medical College of Georgia and Augusta Veterans Affairs Medical Center, Augusta, GA, 30912-3175, USA). Methods in Enzymology, 329(Regulators and Effectors of Small GTPases, Part E), 225-234 (English) 2001. CODEN: MENZAU. ISSN: 0076-6879. Publisher: Academic Press.

AB In Madin-Darby canine kidney (MDCK) cells, Rab25 levels are very low, whereas endogenous Rab11a levels are relatively high. Therefore, to study Rab25 in MDCK cells, cells lines stably transfected with the wild-type sequence of rabbit Rab25. To detect Rab25, monoclonal **antibodies** specific for Rab25, and nonreactive against Rab11a, were also developed. (c) 2001 Academic Press.

L8 ANSWER 11 OF 68 MEDLINE on STN DUPLICATE 5

2001493900 Document Number: 21095781. PubMed ID: 11160825. Structure and function of a vimentin-associated matrix adhesion in endothelial cells. Gonzales M; Weksler B; Tsuruta D; Goldman R D; Yoon K J; Hopkinson S B; Flitney F W; Jones J C. (Department of Cell and Molecular Biology, Northwestern University Medical School, Chicago, Illinois 60611, USA.) MOLECULAR BIOLOGY OF THE CELL, (2001 Jan) 12 (1) 85-100. Journal code: 9201390. ISSN: 1059-1524. Pub. country: United States. Language: English.

AB The alpha4 laminin subunit is a component of endothelial cell basement membranes. An **antibody** (**2A3**) against the alpha4 laminin G domain stains focal contact-like structures in transformed and primary microvascular endothelial cells (TrHBMECs and HMVECs, respectively), provided the latter cells are activated with growth factors. The **2A3 antibody** staining colocalizes with that generated by alphav and beta3 integrin **antibodies** and, consistent with this localization, TrHBMECs and HMVECs adhere to the alpha4 laminin subunit G domain in an alphavbeta3-integrin-dependent manner. The alphavbeta3 integrin/**2A3 antibody** positively stained focal contacts are recognized by vinculin **antibodies** as well as by **antibodies** against plectin. Unusually, vimentin intermediate filaments, in addition to microfilament bundles, interact with many of the alphavbeta3 integrin-positive focal contacts. We have investigated the function of alpha4-laminin and alphavbeta3-integrin, which are at the core of these focal contacts, in cultured endothelial cells. **Antibodies** against these proteins inhibit branching morphogenesis of TrHBMECs and HMVECs in vitro, as well as their ability to repopulate in vitro wounds. Thus, we have characterized an endothelial cell matrix adhesion, which shows complex cytoskeletal interactions and whose assembly is regulated by growth factors. Our data indicate that this adhesion structure may play a role in angiogenesis.

L8 ANSWER 12 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
2000:224579 Document No.: PREV200000224579. Role of the alpha4 laminin subunit in endothelial cell-matrix adhesions and angiogenesis. Gonzales, M. [Reprint author]; Jones, J. C. R. [Reprint author]. North-western University Medical School, Chicago, IL, USA. Journal of Investigative Dermatology, (April, 2000) Vol. 114, No. 4, pp. 821. print.
Meeting Info.: 61st Annual Meeting of the Society for Investigative Dermatology. Chicago, Illinois, USA. May 10-14, 2000.
CODEN: JIDEAE. ISSN: 0022-202X. Language: English.

L8 ANSWER 13 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 6
2001:77532 Document No.: PREV200100077532. Occurrence of Citrus psorosis virus in Campania, southern Italy. Alioto, D. [Reprint author]; Troisi, A. [Reprint author]; Peluso, A. [Reprint author]; Quatrano, G. [Reprint author]; Masenga, V.; Milne, R. G.. Department of Plant Pathology, University of Portici, Portici, I-80055, Naples, Italy. alioto@unina.it. European Journal of Plant Pathology, (October, 2000) Vol. 106, No. 8, pp. 795-799. print.
ISSN: 0929-1873. Language: English.
AB Citrus psorosis virus (CPsV), genus Ophiovirus, is associated with a severe disease of citrus worldwide. Double **antibody** sandwich (DAS) ELISA using a polyclonal antiserum, and triple **antibody** sandwich (TAS) ELISAs, employing the IgG monoclonal **antibody** (mab) 13C5, and the IgM mab **2A3**, were used to detect CPsV in orchards of different citrus varieties in Campania, southern Italy. TAS ELISA with 13C5 detected all the infections detected by DAS ELISA. Overall, 14% of trees younger than 15 years were positive, but only 1% of older trees, suggesting that infected propagating material has been increasingly used in recent years, in the absence of certification. Highest infection rates were in younger trees of sweet orange (22.8%) and clementine (18.6%). CPsV could easily be detected at all seasons of the year tested (June-January); these and earlier results indicate that TAS ELISA using 13C5 is a sensitive, broad-spectrum and reliable diagnostic method useful for routine tests and certification programmes. Of 44 field isolates responding strongly to DAS ELISA and 13C5-TAS ELISA, mab **2A3** gave similar results with 29 isolates, but gave low values with the others, thus providing a degree of differentiation among isolates. To confirm that the ELISA tests were indeed detecting CPsV, samples of 42 ELISA-positive plants were analysed by ISEM in a blind test,

and in 38 of these, characteristic virus particles were clearly seen. Although CPsV was frequently and consistently detected in the area sampled, bark scaling symptoms were not seen: possible reasons for this are discussed.

L8 ANSWER 14 OF 68 MEDLINE on STN DUPLICATE 7
2001104244 Document Number: 21010412. PubMed ID: 11127290. Evolution of alachlor-induced nasal neoplasms in the Long-Evans rat. Genter M B; Burman D M; Dingeldein M W; Clough I; Bolon B. (Department of Environmental Health, University of Cincinnati, Ohio 45267-0056, USA.. MaryBeth.Genter@UC.edu) . TOXICOLOGIC PATHOLOGY, (2000 Nov-Dec) 28 (6) 770-81. Journal code: 7905907. ISSN: 0192-6233. Pub. country: United States. Language: English.

AB The chloracetanilide herbicide alachlor (2-chloro-2',6-diethyl-N-(methoxymethyl)-acetanilide) induces nasal neoplasms in rats following chronic dietary exposure. The present study sought to identify the cellular origin and mechanisms of tumor induction and progression. Male Long-Evans rats were fed alachlor (0 or 126 mg/kg/day) beginning at 6 weeks of age. Following 1 month of alachlor ingestion, neither histological abnormalities nor enhanced cell division (assessed by BrdU incorporation) occurred in any region of the nasal cavity. Six months of alachlor exposure resulted in proliferation of basal and nonbasal cells in the olfactory mucosa while inducing nasal masses in 7 of 15 animals. Tumors ranged from dysplastic plaques to polypoid adenomas and originated in the olfactory regions of the nasal cavity. Neoplasms were associated with regions of respiratory metaplasia and were often covered with a low cuboidal, poorly ciliated epithelium. Tumor cells did not express characteristics of the olfactory mucosa, including olfactory marker protein (OMP, for neurons) and NMa (**antibody** recognizing cytochrome P450 [CYP] **2A3**, found in Bowman's glands). Sites of plaque and tumor development coincided with regions of NMa immunoreactivity. These data suggest that local metabolism is important in alachlor-induced olfactory tumors and support the concept that metaplastic respiratory epithelial cells give rise to the observed neoplasms.

L8 ANSWER 15 OF 68 MEDLINE on STN DUPLICATE 8
1999437836 Document Number: 99437836. PubMed ID: 10508077. Production and characterization of monoclonal **antibodies** against the hemolysin BL enterotoxin complex produced by Bacillus cereus. Dietrich R; Fella C; Strich S; Martlbauer E. (Institute for Hygiene and Technology of Food of Animal Origin, Veterinary Faculty, University of Munich, 80539 Munich, Germany.) APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (1999 Oct) 65 (10) 4470-4. Journal code: 7605801. ISSN: 0099-2240. Pub. country: United States. Language: English.

AB A total of five hybridoma cell lines that produced monoclonal **antibodies** against the components of the hemolysin BL (HBL) enterotoxin complex and sphingomyelinase produced by Bacillus cereus were established and characterized. Monoclonal **antibody 2A3** was specific for the B component, **antibodies** 1A12 and 8B12 were specific for the L(2) component, and **antibody** 1C2 was specific for the L(1) protein of the HBL enterotoxin complex. No cross-reactivity with other proteins produced by different strains of B. cereus was observed for monoclonal **antibodies 2A3**, 1A12, and 8B12, whereas **antibody** 1C2 cross-reacted with an uncharacterized protein of approximately 93 kDa and with a 39-kDa protein, which possibly represents one component of the nonhemolytic enterotoxin complex. **Antibody** 2A12 finally showed a distinct reactivity with B. cereus sphingomyelinase. The monoclonal **antibodies** developed in this study were also successfully applied in indirect enzyme immunoassays for the characterization of the enterotoxic activity of B. cereus strains. About 50% of the strains tested were capable of producing the HBL enterotoxin complex, and it could be demonstrated that all strains producing HBL were also highly cytotoxic.

L8 ANSWER 16 OF 68 MEDLINE on STN DUPLICATE 9
2000072588 Document Number: 20072588. PubMed ID: 10604876.
N-Nitrosobenzylmethylamine hydroxylation and coumarin 7-hydroxylation: catalysis by rat esophageal microsomes and cytochrome P450 **2A3** and 2A6 enzymes. von Weymarn L B; Felicia N D; Ding X; Murphy S E. (Department of Biochemistry, Molecular Biology and Biophysics, University of Minnesota Cancer Center, Minneapolis, Minnesota 55455, USA.) CHEMICAL RESEARCH IN TOXICOLOGY, (1999 Dec) 12 (12) 1254-61. Journal code: 8807448. ISSN: 0893-228X. Pub. country: United States. Language: English.

AB N-Nitrosobenzylmethylamine (NBzMA) is a potent and selective esophageal carcinogen in the rat and may be a causative agent for human esophageal cancer. This nitrosamine, like most, must be metabolically activated to exert its carcinogenic potential. NBzMA may be metabolized by P450-catalyzed methyl or methylene hydroxylation; the latter is believed to be the activation pathway. The sensitivity of the esophagus to NBzMA-induced tumorigenesis is believed to be due, at least in part, to the presence of efficient P450 catalysts in this tissue. However, while it was reported almost 20 years ago that the rat esophagus catalyzes the methylene hydroxylation of NBzMA, the P450 that catalyzes this reaction has yet to be identified. We report here that human P450 2A6 and the closely related extrahepatic rat enzyme P450 **2A3** both efficiently catalyze NBzMA methylene hydroxylation, characterized as benzaldehyde formation. The catalytic efficiency of P450 **2A3** in this reaction was 3-fold greater than that of P450 2A6, 7.6 (K(m) = 0.63 +/- 0.18 microM and the V(max) = 4.8 nmol min(-)(1) nmol of P450(-)(1)) versus 2.3 (K(m) = 6.7 +/- 2.9 microM and the V(max) = 15.7 nmol min(-)(1) nmol of P450(-)(1)), respectively. Both enzymes catalyzed methylene hydroxylation at least 4-fold more efficiently than methyl hydroxylation. In addition, P450 2A6, but not P450 **2A3**, catalyzed benzyl ring hydroxylation, generating N-(p-hydroxybenzyl)methylamine. The identity of this metabolite was confirmed by synthesis of a standard and LC/MS and LC/MS/MS analysis. P450 2A6 is an efficient coumarin 7-hydroxylase, and we report here that P450 **2A3** is an equally good catalyst of this reaction (K(m) = 1. 7 +/- 0.41 microM and V(max) = 1.7 +/- 0.08 nmol min(-)(1) nmol of P450(-)(1)). Rat esophageal microsomes (REM), like P450 **2A3**, were efficient catalysts of NBzMA methylene hydroxylation. However, in contrast to P450 **2A3**, the major product of this reaction was the product of benzaldehyde oxidation, benzoic acid. **Antibody** to the closely related mouse P450, 2A5, did not inhibit REM-catalyzed NBzMA metabolism, and most importantly, REM did not catalyze the 7-hydroxylation of coumarin. Therefore, P450 **2A3** does not appear to be the P450 in the rat esophagus responsible for catalyzing the methylene hydroxylation of NBzMA.

L8 ANSWER 17 OF 68 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
1999:846819 The Genuine Article (R) Number: 250ZA. Pathophysiology and treatment of graft-versus-host disease. Flowers M E D (Reprint); Kansu E; Sullivan K M. FRED HUTCHINSON CANC RES CTR, 1100 FAIRVIEW AVE N, FM-252, SEATTLE, WA 98109 (Reprint); UNIV WASHINGTON, SCH MED, SEATTLE, WA; UNIV HACETTEPE, INST ONCOL, DEPT MED, TR-06100 ANKARA, TURKEY; DUKE UNIV, DEPT MED, DIV MED ONCOL & TRANSPLANTAT, DURHAM, NC. HEMATOLOGY-ONCOLOGY CLINICS OF NORTH AMERICA (OCT 1999) Vol. 13, No. 5, pp. 1091-&. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0889-8588. Pub. country: USA; TURKEY. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Acute graft-versus-host disease denotes a distinctive syndrome characterized by a triad of dermatitis (rash), hepatitis (jaundice), and gastroenteritis (abdominal pain, diarrhea) developing in the first 100 days after allogeneic hematopoietic cell transplantation. Chronic graft-versus-host disease designates a more diverse syndrome, usually presenting with multiorgan involvement and commonly developing 100 days after hematopoietic cell transplantation. This article discusses the

pathophysiology, incidence and predictive factors, clinical manifestations, diagnosis and grading, prevention, and treatment for both types of the disease.

L8 ANSWER 18 OF 68 MEDLINE on STN DUPLICATE 10
1999265376 Document Number: 99265376. PubMed ID: 10334207. Expression of cytochrome P450 **2A3** in rat esophagus: relevance to N-nitrosobenzylmethylamine. Gopalakrishnan R; Morse M A; Lu J; Weghorst C M; Sabourin C L; Stoner G D; Murphy S E. (Department of Pathology, College of Medicine and Public Health, The Ohio State University, Columbus 43210, USA.) CARCINOGENESIS, (1999 May) 20 (5) 885-91. Journal code: 8008055. ISSN: 0143-3334. Pub. country: ENGLAND: United Kingdom. Language: English.

AB N-nitrosobenzylmethylamine (NBzMA) must be metabolically activated to exert its carcinogenic potential and is a potent inducer of tumors in the rat esophagus. The activation is believed to occur in the esophagus. Although the pathways of NBzMA metabolism are well studied, the principal cytochrome P450 enzyme(s) (P450) responsible for catalyzing its activation is unknown. Several preliminary studies have suggested that this enzyme may belong to the P450 2A family. We report here that P450 **2A3** expressed in a baculovirus system metabolizes NBzMA, predominantly by methylene hydroxylation. To determine whether or not P450 **2A3** is present in the rat esophagus, the relative level of P450 **2A3** mRNA was determined by reverse transcriptase-polymerase chain reaction (RT-PCR). The mRNA levels of P450 **2A3** were compared with the levels of P450 2A1 and 2A2 mRNA in the esophagus, liver, lung and nasal mucosa. P450 **2A3** mRNA was detected in rat nasal mucosa, lung and esophagus, but not in liver, whereas P450 2A1 and 2A2 mRNAs were detected only in the liver. To determine the relative expression of P450 **2A3** in each tissue, quantitative RT-PCR with PCR-MIMICS used as internal standards was performed. The expression level in the nasal mucosa was by far the greatest. The expression in the lung and esophagus was 60- and 1600-fold less, respectively. Using **antibodies** to P450 2A4/5 and P450 2A10/11 a 50 kDa immunoreactive protein was detected in all three tissues by western blot analysis. This is consistent with the expression of P450 **2A3** in these tissues. However, the amount of protein detected in the nasal mucosa was much greater than that in the esophagus or lung. The expression of P450 2A protein was similar in the lung and esophagus. The rate of coumarin 7-hydroxylation in cultured rat esophagus was very low. This is a reaction efficiently catalyzed by P450 2A5, 2A6 and 2A10. In summary, our results clearly demonstrate the presence of P450 **2A3** protein and mRNA in the esophagus, but the amounts are low and may not be sufficient to account for NBzMA activation in this tissue.

L8 ANSWER 19 OF 68 CAPLUS COPYRIGHT 2003 ACS on STN
1999:65703 Document No. 130:250394 A novel member of the NF2/ERM/4.1 superfamily with growth suppressing properties in lung cancer. Tran, Yen K.; Bogler, Oliver; Gorse, Karen M.; Wieland, Ilse; Green, Mark R.; Newsham, Irene F. (University of California-San Diego Cancer Center, University of California-San Diego, La Jolla, CA, 92093, USA). Cancer Research, 59(1), 35-43 (English) 1999. CODEN: CNREA8. ISSN: 0008-5472. Publisher: AACR Subscription Office.

AB A novel putative tumor suppressor gene and member of the NF2/ERM/ 4.1 superfamily was isolated using Differential Display PCR (DDPCR) on primary lung tumors. When reintroduced into nonexpressing non-small cell lung carcinoma cell lines, this gene, named DAL-1 (for Differentially expressed in Adenocarcinoma of the Lung), was shown to suppress growth. In addn., significantly reduced expression (>50%) of DAL-1 was measured in 39 primary non-small cell lung carcinoma tumors as compared with patient-matched normal lung tissue. Immunocytochem. staining with a polyclonal anti-DAL-1 **antibody** localized the protein to the plasma membrane, particularly at cell-cell contact points, a pattern reminiscent of other members of the protein 4.1 superfamily including ezrin and NF2. The data suggest DAL-1 is a novel membrane-assocd. protein

with potential to play an important role in the origin and progression of lung cancer.

L8 ANSWER 20 OF 68 MEDLINE on STN DUPLICATE 11
1998194279 Document Number: 98194279. PubMed ID: 9533085. Detection and classification of infectious bronchitis viruses isolated in Korea by dot-immunoblotting assay using monoclonal **antibodies**. Song C S; Kim J H; Lee Y J; Kim S J; Izumiya Y; Tohya Y; Jang H K; Mikami T. (National Veterinary Research Institute, RDA, Anyang, Korea.) AVIAN DISEASES, (1998 Jan-Mar) 42 (1) 92-100. Journal code: 0370617. ISSN: 0005-2086. Pub. country: United States. Language: English.

AB Dot-immunoblotting assay (DIA) using five monoclonal **antibodies** (MAbs) to infectious bronchitis virus (IBV) was used to detect and classify the viruses propagated in embryonated chicken eggs. Using a group-specific MAb 3F5, 10 reference strains and 12 Korean isolates of IBV were successfully detected by DIA, and the lowest virus titer of IBV detected by DIA was approximately less than 10(3.8) mean embryo infective dose/ml. For evaluating the diagnostic efficiency, DIA was compared with the conventional infectious bronchitis (IB) diagnostic method. IBV antigens in allantoic fluid from embryonated eggs inoculated with IB-suspected field samples were specifically detected by DIA within only one or two egg passages, whereas the conventional embryonated egg inoculation method required four to seven egg passages for confirming IBV infection. These results indicated that DIA could significantly reduce time and cost for IB diagnosis. For examining the possibility of classifying IBV by DIA, four strain-specific MAbs, 3A4, **2A3**, 6F7, and 2C6, were used. According to the MAb reacting patterns to the IBV antigens, the 10 IBV reference strains were classified into six groups; seven strains belonged to three different groups, and the other three strains each belonged to an individual group. In the case of 12 Korean isolates of IBV, they were classified in six groups. Among the six groups, the MAb reacting patterns of three groups matched those of the IBV reference strains, but the others did not. These data suggest that at least three variant serotypes of IBV exist in Korea.

L8 ANSWER 21 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
1997:118355 Document No.: PREV199799417558. Transient expression of Dp140, a product of the Duchenne muscular dystrophy locus, during kidney tubulogenesis. Durbeej, Madeleine [Reprint author]; Jung, Daniel; Hjalt, Tord [Reprint author]; Campbell, Kevin P.; Ekblom, Peter [Reprint author]. Dep. Animal Physiology, Uppsala Univ., Uppsala, Sweden. Developmental Biology, (1997) Vol. 181, No. 2, pp. 156-167.
CODEN: DEBIAO. ISSN: 0012-1606. Language: English.

AB Dystroglycan is a cell surface complex which in muscle links the extracellular matrix protein laminin-2 to the membrane associated cytoskeletal protein dystrophin. Recently it was found that dystroglycan is also expressed in developing epithelial cells. Moreover, **antibodies** against dystroglycan can perturb epithelial cell development in kidney organ culture. Dystroglycan could provide a link between the basement membrane and the intracellular space also in epithelial cells. However, there is no dystrophin in epithelial cells. By in situ hybridization here we show prominent expression of a shorter isoform of dystrophin, Dp140, in embryonic kidney tubules. In addition, another isoform, Dp71, is expressed by all studied embryonic epithelial cells. Both isoforms share the dystroglycan-binding region of dystrophin but lack the region known to bind to actin. Here we also characterized monoclonal **antibodies** against different domains of dystrophin and used these to study the distribution of Dp140 protein. In embryonic kidney tubules the dystrophin **antibody** VIA4-**2A3** stained an intracellular antigen close to the basal cells. in contrast, no staining was observed in adult kidney. We suggest that Dp140 is a structural component during kidney tubulogenesis but it may also be involved in signal transduction.

L8 ANSWER 22 OF 68 MEDLINE on STN DUPLICATE 12
1998035439 Document Number: 98035439. PubMed ID: 9368964. Detection of Mycoplasma mycoides subspecies mycoides by growth-inhibition using monoclonal **antibodies**. Rodriguez F; Fernandez A; Ball H J. (Department of Animal Pathology, Faculty of Veterinary Medicine, Las Palmas de Gran Canaria, Spain.) RESEARCH IN VETERINARY SCIENCE, (1997 Jul-Aug) 63 (1) 91-2. Journal code: 0401300. ISSN: 0034-5288. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A pool of three monoclonal **antibodies**, 3H12, 6D11 and **2A3**, inhibited the in vitro growth of 12 Mycoplasma mycoides subspecies mycoides small colony (MmmSC) strains and seven Mycoplasma mycoides subspecies mycoides large colony (MmmLC) strains. This test did not cross-react with other 16 Mycoplasma mycoides cluster and nine non-Mycoplasma mycoides cluster strains representing 13 different species. Although MmmSC was not differentiated from MmmLC, the monoclonal **antibodies** distinguished both M mycoides subspecies mycoides biotypes from the other Mycoplasma species tested in contrast to results with polyclonal antisera.

L8 ANSWER 23 OF 68 MEDLINE on STN DUPLICATE 13
97040369 Document Number: 97040369. PubMed ID: 8885707. An immunohistochemical method of detecting Mycoplasma species antigens by use of monoclonal **antibodies** on paraffin sections of pneumonic bovine and caprine lungs. Rodriguez F; Kennedy S; Bryson T D; Fernandez A; Rodriguez J L; Ball H J. (Department of Agriculture for Northern Ireland, Veterinary Sciences Division, Belfast.) ZENTRALBLATT FUR VETERINARMEDIZIN. REIHE B, (1996 Sep) 43 (7) 429-38. Journal code: 0331325. ISSN: 0514-7166. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Lung samples from pneumonic lesions in cattle and goats, naturally or experimentally infected with strains of the Mycoplasma mycoides cluster, were fixed in formalin and embedded in paraffin. An immunohistochemical technique using monoclonal or polyclonal **antibodies** was performed on tissue sections in order to detect Mycoplasma antigens. Four monoclonal **antibodies** (MAbs), one (**2A3**) raised against M. mycoides ssp. mycoides small colony (SC) and large colony (LC), two (1D3 and 5E5) against M. mycoides ssp. capri, and one (5A10) against M. bovis, were used. A range of polyclonal **antibodies**, raised to the individual subspecies of the M. mycoides cluster, and one to Pasteurella haemolytica, was also used. The MAb **2A3** showed positive immunostaining in lung sections from cattle and goats naturally and experimentally infected with M. mycoides ssp. mycoides SC and LC, but not with pneumonic lesions of cattle and goats due to other members of the M. mycoides cluster, M. bovis or Pasteurella spp. The MAb 1D3 showed immunostaining in lung sections from goats naturally and experimentally infected with M. mycoides ssp. capri, but again not with pneumonic lesions caused by other members of the M. mycoides cluster, M. bovis or Pasteurella spp. The MAb 5E5 immunoreacted in sections from pneumonic lesions from all animals infected with one of the three M. mycoides cluster subspecies used in the study, but not with M. bovis or Pasteurella infected tissue. Immunoreaction was mainly found in the cell debris around necrotic areas, as well as in macrophages, neutrophils and epithelial cells. The localization of antigens of the M. mycoides cluster using polyclonal antisera followed basically the same pattern as that obtained with the monoclonals. However, a wide cross reactivity was found between different antisera and relatively high background immunostaining was also seen, especially in necrotic areas. The results suggest that immunohistochemical methods using monoclonal **antibodies** are useful tools for the diagnosis and study of the pathogenesis of pneumonia caused by the Mycoplasmas of the M. mycoides cluster.

L8 ANSWER 24 OF 68 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
96:703306 The Genuine Article (R) Number: VH772. AN IMMUNOHISTOCHEMICAL METHOD OF DETECTING MYCOPLASMA SPECIES ANTIGENS BY USE OF MONOCLONAL-

ANTIBODIES ON PARAFFIN SECTIONS OF PNEUMONIC BOVINE AND CAPRINE LUNGS. RODRIGUEZ F (Reprint); KENNEDY S; BRYSON T D G; FERNANDEZ A; RODRIGUEZ J L; BALL H J. DEPT AGR NO IRELAND, VET SCI DIV, STONEY RD, BELFAST BT4 3SD, ANTRIM, NORTH IRELAND (Reprint). JOURNAL OF VETERINARY MEDICINE SERIES B-ZENTRALBLATT FUR VETERINARMEDIZIN REIHE B-INFECTIOUS DISEASES AND VETERINARY PUBLIC HEALTH (SEP 1996) Vol. 43, No. 7, pp. 429-438. ISSN: 0931-1793. Pub. country: NORTHERN IRELAND. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Lung samples from pneumonic lesions in cattle and goats, naturally or experimentally infected with strains of the Mycoplasma mycoides cluster, were fixed in formalin and embedded in paraffin. An immunohistochemical technique using monoclonal or polyclonal **antibodies** was performed on tissue sections in order to detect Mycoplasma antigens. Four monoclonal **antibodies** (MAbs), one (**2A3**) raised against M. mycoides ssp. mycoides small colony (SC) and large colony (LC), two (1D3 and 5E5) against M. mycoides ssp. capri, and one (5A10) against M. bovis, were used. A range of polyclonal **antibodies**, raised to the individual subspecies of the M. mycoides cluster, and one to Pasteurella haemolytica, was also used. The MAb **2A3** showed positive immunostaining in lung sections from cattle and goats naturally and experimentally infected with M. mycoides ssp. mycoides SC and LC, but not with pneumonic lesions of cattle and goats due to other members of the M. mycoides cluster, M. bovis or Pasteurella spp. The MAb 1D3 showed immunostaining in lung sections from goats naturally and experimentally infected with M. mycoides ssp. capri, but again not with pneumonic lesions caused by other members of the M. mycoides cluster, M. bovis or Pasteurella spp. The MAb 5E5 immunoreacted in sections from pneumonic lesions from all animals infected with one of the three M. mycoides cluster subspecies used in the study, but not with M. bovis or Pasteurella infected tissue. Immunoreaction was mainly found in the cell debris around necrotic areas, as well as in macrophages, neutrophils and epithelial cells. The localization of antigens of the M. mycoides duster using polyclonal antisera followed basically the same pattern as that obtained with the monoclonals. However, a wide cross reactivity was found between different antisera and relatively high background immunostaining was also seen, especially in necrotic areas. The results suggest that immunohistochemical methods using monoclonal **antibodies** are useful tools for the diagnosis and study of the pathogenesis of pneumonia caused by the Mycoplasmas of the M. mycoides cluster.

L8 ANSWER 25 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

96153253 EMBASE Document No.: 1996153253. Generation of monoclonal **antibodies** specific to mesothelioma. Narumi K.; Watanabe H.; Sakakibara N.; Chen F.-A.; Bankert R.B.; Takita H.. Department of First Surgery, Juntendo University, 2-1-1 Hongo,Bunkyo-ku, Tokyo 113, Japan. Biotherapy 10/3 (356-359) 1996.
ISSN: 0914-2223. CODEN: BITPE. Pub. Country: Japan. Language: Japanese. Summary Language: English; Japanese.

AB In attemp to develop mesothelioma specific McAb in our laboratory, spleen cells a mouse immunized with isolated tumor cells from a fresh mesothelioma specimen were fused to a drug resistant mouse myeloma cell lines or mesothelioma tumor biopsy tissues. Two monoclonal **antibodies**, **2A3** and $e1, were identified that bound 6/7 of the mesotheliomas tested, but failed to bind to the majority, 11/13 (for 4E1), of other lung tumors. Based upon western blot analysis of one-and two-dimensional gels and upon the distribution pattern of the **antibody**-recognized molecule, the **2A3 antibody** binds to the cell adhesion molecule CD44. While the specificity of 4E1 has not yet been unequivocally established, it appears to recognize a variant form of the CD44 molecule. Those two monoclonal **antibodies** are not specific to mesothelioma but useful for differential diagnosis between meosthelioma and other tumors of the lung.

L8 ANSWER 26 OF 68 MEDLINE on STN DUPLICATE 14
97057125 Document Number: 97057125. PubMed ID: 8901464. Functional antagonism by a monoclonal **antibody** to digoxin in a test system of cultured rat heart myocytes. Wallukat G; Simon H U; Muller W D; Wolf I. (Max Delbruck Centre for Molecular Medicine, Berlin-Buch, Germany.) MOLECULAR AND CELLULAR BIOCHEMISTRY, (1996 Jul-Aug) 160-161 117-20. Journal code: 0364456. ISSN: 0300-8177. Pub. country: Netherlands. Language: English.

AB A monoclonal **antibody** with a high affinity for digitoxin (KA = 0.50 nM) and digoxin (KA = 0.55 nM) was produced by somatic cell fusion. This **antibody**, designated **2A3**(47), displayed little cross reactivity with other glycosides. In cultured rat heart myocytes, **2A3**(47), antagonized the positive chronotropic effect exerted by digitoxin but did not alter that of ouabain. Our results suggest that this monoclonal **antibody** may prove to be useful in treating digoxin and digitoxin intoxication.

L8 ANSWER 27 OF 68 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
96:764991 The Genuine Article (R) Number: VM242. FUNCTIONAL ANTAGONISM BY A MONOCLONAL-**ANTIBODY** TO DIGOXIN IN A TEST SYSTEM OF CULTURED RAT-HEART MYOCYTES. WALLUKAT G (Reprint); SIMON H U; MULLER W D; WOLF I. MAX DELBRUCK CTR MOL MED, ROBERT ROSSLE STR 10, D-13125 BERLIN, GERMANY (Reprint); UNIV JENA, INST CLIN IMMUNOL, D-07740 JENA, GERMANY. MOLECULAR AND CELLULAR BIOCHEMISTRY (JUL/AUG 1996) Vol. 161, pp. 117-120. ISSN: 0300-8177. Pub. country: GERMANY. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A monoclonal **antibody** with a high affinity for digitoxin (K-A = 0.50 nM) and digoxin (K-A = 0.55 nM) was produced by somatic cell fusion. This **antibody**, designated **2A3**(47), displayed little cross reactivity with other glycosides. In cultured rat heart myocytes, **2A3**(47), antagonized the positive chronotropic effect exerted by digitoxin but did not alter that of ouabain. Our results suggest that this monoclonal **antibody** may prove to be useful in treating digoxin and digitoxin intoxication.

L8 ANSWER 28 OF 68 MEDLINE on STN DUPLICATE 15
96258193 Document Number: 96258193. PubMed ID: 8674240. Expression of selectins (CD62 E,L,P) and cellular adhesion molecules in primary Sjogren's syndrome: questions to immunoregulation. Aziz K E; McCluskey P J; Wakefield D. (School of Pathology, University of New South Wales, Sydney, Australia.) CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (1996 Jul) 80 (1) 55-66. Journal code: 0356637. ISSN: 0090-1229. Pub. country: United States. Language: English.

AB Adhesion molecules are important signal transmitters of the immune system and may mediate the homing of leukocytes to sites of inflammation. The aim of this work was to examine the presence of selecting and cellular adhesion molecules on epithelial and endothelial cells in labial salivary glands (LSG) in Sjogren's syndrome (SS). LSG biopsies were obtained from patients with primary SS (n = 31) and normal subjects (n = 21). Cryostat sections were examined with indirect immunoperoxidase. Epithelial cells in LSG from both patients and controls expressed LFA-3 (CD58) and Hermes I (CD44). A significantly increased number of acinar and ductal epithelial cells in LSG from patients expressed class I MHC (74%, as mean percentage of ductal epithelial cells) ($P < 0.05$), HLA-DR (58%) ($P < 0.0001$), and HLA-DQ (11%) ($P < 0.001$). To a lesser extent limited ICAM-1 (CD54) epithelial expression (6%) was noted only in a few biopsies from patients but none of the controls. Epithelial cells did not express any of the selectins CD62 E, L, and P and sometimes they expressed sialyl Le(x) (a ligand for selectins). Although the number of endothelial structures expressing ICAM-1 (CD54), HLA-DR, HLA-DQ, and class I MHC (per surface area) was increased in patients ($P < 0.05$), this may be due to the total increase of number of endothelial structures ($P < 0.05$) (Von Willebrand factor +ve) as part of the chronic inflammatory process. A smaller

proportion of endothelial structures expressed E-selectin (CD62 E) (32%) and to a lesser extent VCAM-1 (CD106) (approximately 7%) as detectable only in some LSG from patients. P-selectin (CD62 P) was demonstrated on about one-third of endothelial structures in LSG from patients. Infiltrating mononuclear cells expressed CD11a (68%), CD18 (73%), CD11b (13%), CD11c (21%), CD58 (13%), CD4 (44%), CD8 (17%), CD62L (L-selectin) (18%), CD49d (38%), CD49e (15%), CD2 (56%), and CD44 (77%). The relatively reduced number of CD62 L +ve lymphocytes may be due to shedding of that molecule after activation. Sialyl Le(x) was not detectable on infiltrating lymphocytes. Although infiltrating mononuclear cells were activated, as evidenced by their expression of HLA-DR (72%) and ICAM-1 (55%), they did not express IL-2Ralpha (CD25, confirmed by two **antibodies 2A3** and ACT1) or IL-2Rbeta (CD122), except rarely (< or = 1%). In some biopsies, CD106 and CD11c were localized on lymphocytes at the central areas of periductal lymphoid follicles with the appearance of dendritic cells. We conclude that adhesion molecules probably play a major role in the pathogenesis of SS. The pattern of expression of these molecules demonstrates a regulated altered activation in the glands associated with this disease. The glands may be subject to specific regulatory factors, in addition to proinflammatory cytokines.

L8 ANSWER 29 OF 68 MEDLINE on STN
96176425 Document Number: 96176425. PubMed ID: 8598142. **2A3** and 3F9. Novel lung epithelial antigens with early upregulation in hyperoxic and radiation lung injury models. Girod C E; Shin D H; Hershenson M B; Solway J; Redlich C A; Gilman L B; Miller Y E. (University of Colorado Health Sciences Center, Denver, USA.) CHEST, (1996 Mar) 109 (3 Suppl) 33S. Journal code: 0231335. ISSN: 0012-3692. Pub. country: United States. Language: English.

L8 ANSWER 30 OF 68 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
95:443228 The Genuine Article (R) Number: RE631. LYMPHOCYTE-DERIVED CYTOKINES AUGMENT MACROPHAGE TUMOR-NECROSIS-FACTOR-ALPHA AND INTERLEUKIN-6 SECRETION DURING EXPERIMENTAL GRAM-NEGATIVE BACTERIAL SEPSIS. BATTAFARANO R J (Reprint); KIM S K; DAHLBERG P S; FARBER M S; RATZ C A; JOHNSTON J W; DUNN D L. UNIV MINNESOTA, DEPT SURG, DIV SURG INFECT DIS, MINNEAPOLIS, MN, 55455 (Reprint). JOURNAL OF SURGICAL RESEARCH (JUN 1995) Vol. 58, No. 6, pp. 739-745. ISSN: 0022-4804. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Although lymphocyte-derived cytokines are known to augment macrophage cytokine production in vitro, their effect on macrophage tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6) secretion during gram-negative bacterial sepsis has not been characterized. The purpose of this study was to examine the effect of lymphocyte-derived cytokines on macrophage TNF-alpha and IL-6 secretion during gram-negative bacterial peritonitis. To examine this problem, uninfected and infected mice were studied. Mice were infected with Escherichia coil 0111:B4 and two subgroups were examined consisting of those pretreated iv 1 hr prior to bacterial challenge with either (1) saline or (2) anti-E. coil 0111:B4 LPS mAb **2A3**, the latter administered to abrogate the effects of LPS in vivo. Thus, three groups of mice were studied in relation to pretreatment and infectious challenges: (1) saline/saline (control); (2) saline/E. coil (saline); and (3) mAb **2A3**/E. coil (mAb **2A3**). Nonadherent splenocytes (>95% lymphocytes by histologic staining criteria) harvested 16 hr later from mice in each group were incubated in culture ex vivo for 3 hr to obtain supernatants containing lymphocyte-derived cytokines. These supernatants containing lymphocyte-derived cytokines then were incubated in vitro with naive splenic macrophages with or without E. coli 0111:B4 LPS. Macrophage TNF-alpha and IL-6 levels were determined using L929 and B9 bioassays. Lymphocyte-derived cytokines obtained 16 hr after infection from mice pretreated with saline significantly stimulated TNF-alpha and IL-6 secretion compared to those obtained from uninfected mice (TNF-alpha, 525 +/- 67 pg/ml versus 16 +/- 03 pg/ml, P < 0.001; IL-6, 19.2 +/- 7.7 ng/ml

versus 1.5 +/- 0.0 ng/ml, P < 0.05) and synergistically enhanced macrophage TNF-alpha secretion in combination with LPS compared to that in medium (1601 +/- 378 pg/ml versus 850 +/- 146 pg/ml, P < 0.05). Pretreatment of infected animals with anti-LPS mAb **2A3** blocked this effect (525 +/- 67 pg/ml versus 183 +/- 73 pg/ml, P < 0.01; 1601 +/- 378 pg/ml versus 791 +/- 46 pg/ml, P < 0.05). Interferon-gamma (IFN-gamma) concentrations in the lymphocyte-derived cytokines of all groups were <35 pg/ml. Thus, LPS released during infection induces lymphocytes to secrete cytokines other than IFN-gamma that may act to amplify the host cytokine response. Characterization of the cytokines responsible for this phenomenon may prove important in further delineating the pathophysiology of the host septic response. (C) 1995 Academic Press, Inc.

L8 ANSWER 31 OF 68 MEDLINE on STN DUPLICATE 16

96082436 Document Number: 96082436. PubMed ID: 7583936. Heterogeneity of VP4 neutralization epitopes among serotype P1A human rotavirus strains. Contreras J F; Menchaca G E; Padilla-Noriega L; Tamez R S; Greenberg H B; Lopez S; Arias C F. (Departamento de Microbiologia e Inmunologia, Facultad de Ciencias Biologicas, Universidad Autonoma de Nuevo Leon, Mexico.) CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (1995 Jul) 2 (4) 506-8. Journal code: 9421292. ISSN: 1071-412X. Pub. country: United States. Language: English.

AB We have used serotype-specific VP4 and VP7 neutralizing monoclonal **antibodies** (Nt-MAbs), as well as subgroup (SG)-specific MAbs, to characterize by enzyme immunoassay rotavirus strains isolated from diarrheic infants in the city of Monterrey, Mexico, from July 1993 to March 1994. Of a total of 465 children studied, 140 were rotavirus positive, including 3 patients infected with non-group A rotaviruses. The SG and VP7 (G) serotype specificities could be determined for 118 (84%) of the 140 rotavirus-positive stool specimens; 4 rotavirus strains were serotype G1 and SGII; 1 strain was serotype G2 and SGI+II; 112 strains were serotype G3 and SGII; 1 strain was serotype G3 and SGI; and none of the strains was serotype G4. Fifty-eight specimens, representing the 13 different group A rotavirus electropherotypes detected, were chosen for VP4 (P) serotyping. Of these, 48 (83%) strains reacted with the P1A serotype-specific Nt-MAb 1A10. None of the strains reacted with the serotype P2-specific Nt-MAbs tested. Not all viruses that reacted with Nt-MAb 1A10 were recognized by Nt-MAbs **2A3** and 2G1, which also recognize P1A strains, indicating heterogeneity of neutralization epitopes among serotype P1A human rotaviruses. This heterogeneity could be relevant for the specificity of the VP4-mediated neutralizing **antibody** immune response and indicates the need for antigenic characterization, in addition to genomic typing, of the VP4 proteins of circulating human rotavirus field strains.

L8 ANSWER 32 OF 68 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

95:591776 The Genuine Article (R) Number: RR812. THE TISSUE EXPRESSION OF CYTOKINES IN HUMAN ACUTE CUTANEOUS GRAFT-VERSUS-HOST DISEASE. ROY J (Reprint); BLAZAR B R; OCHS L; WEISDORF D J. UNIV LAVAL, HOP ST SACREMENT, DIV HEMATOL, 1050 CHEMIN SAINTE FOY, QUEBEC CITY, PQ G1S 4L8, CANADA (Reprint); UNIV MINNESOTA, DEPT MED & PEDIAT, MINNEAPOLIS, MN, 55455; UNIV MINNESOTA, BONE MARROW TRANSPLANT PROGRAM, MINNEAPOLIS, MN, 55455. TRANSPLANTATION (27 AUG 1995) Vol. 60, No. 4, pp. 343-348. ISSN: 0041-1337 . Pub. country: CANADA; USA. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Although acute graft-versus-host disease (GVHD) is a common complication after allogeneic bone marrow transplantation (BRIT), the specific pathophysiology of tissue damage has not been elucidated, We have previously described an infiltrate of CD2+, CD8+, alpha/beta receptor(+) T lymphocytes, and the upregulation of ICAM-1 in tissues with acute GVHD, We hypothesized that these infiltrating lymphocytes may secrete cytokines that could contribute to tissue damage, In the current study, we used reverse transcription (RT) polymerase chain reaction (PCR) to explore the mRNA expression of candidate inflammatory cytokines IL-1 alpha, IL-2,

IL-4, IL-6, TNF-alpha, and interferon-gamma (IFN-gamma) in peripheral blood mononuclear cells (PBMC) and skin biopsies of allogeneic BRIT patients with GVHD and controls, In post-BMT control PBMC (n=10), IL-2 RNA was infrequent (20% of samples) but was significantly more frequently detectable (71%; P<0.05) after development of acute GVHD (n=7), IL-4 expression was also more common in PBMC from patients with acute GVHD (57% vs, 30%; P<0.05), Consistent with the PBMC data, IL-2 and IL-4 RNA were also more frequently detectable in skin biopsies with GVHD (n=10): 70% of samples expressed IL-2 vs, 25% of normal controls (n=8; P<0.05); 60% had detectable IL-4 RNA vs, 0% of controls (P<0.05). IFN-gamma detectability (40% vs, 12%; P<0.05) was also more frequent in GVH skin, For both PBMC and skin, IL-1 alpha expression was infrequent in GVHD and controls, whereas TNF-alpha and IL-6 were expressed in nearly all samples, These data suggest that upregulated expression of IL-2, IL-4, and IFN-gamma may be part of the inflammatory cascade of human acute GVHD, while IL-1 alpha, TNF-alpha, and IL-6 are not discriminatory for the inflammation observed at the time of initial GVHD diagnosis.

L8 ANSWER 33 OF 68 EMBASE
on STN
94256750 EMBASE Document No.: 1994256750. Anti-IL-2 receptor **antibody** for prophylaxis and treatment of immunologic reactions after bone marrow and solid organ transplantation. Klingemann H.-G.. Leuk./Bone Marrow Trans. Prog. B.C., Vancouver Hosp. and Health Sci. Ctr., 910 West 10th Avenue,Vancouver, BC V5Z 4E3, Canada. Drugs of the Future 19/7 (659-663) 1994.
ISSN: 0377-8282. CODEN: DRFUD4. Pub. Country: Spain. Language: English.

L8 ANSWER 34 OF 68 MEDLINE on STN
2001170831 Document Number: 21088639. PubMed ID: 11271306. In vitro and in vivo effects of BT 563, an anti-interleukin-2 receptor monoclonal **antibody**. Van Gelder T; Daane C R; Vaessen L M; Hesse C J; Mochtar B; Balk A H; Weimar W. (Department of Internal Medicine, University Hospital Rotterdam, The Netherlands.) TRANSPLANT INTERNATIONAL, (1994) 7 Suppl 1 S556-8. Journal code: 8908516. ISSN: 0934-0874. Pub. country: Germany: Germany, Federal Republic of. Language: English.
AB BT 563, a murine anti-IL-2R MoAb, was found to be more potent than anti-Tac in inhibiting proliferation in the mixed lymphocyte reaction. Results obtained with 33B3.1 in these experiments were similar to those with BT 563. The anti-IL-2R MoAb **2A3** was shown to be a suitable agent for monitoring the effect of BT 563 on peripheral blood. IL-2R-positive cells were not detected in peripheral blood samples from 1 h after the first dose until 8 days after the last dose. Plasma trough levels were measured in patients receiving 5 or 10 mg daily. The administration of BT 563 to allograft recipients did not lead to clinically significant side effects.

L8 ANSWER 35 OF 68 MEDLINE on STN DUPLICATE 17
94137124 Document Number: 94137124. PubMed ID: 8304828. Inhibition of splenic macrophage tumor necrosis factor alpha secretion in vivo by antilipopolysaccharide monoclonal **antibodies**. Battafarano R J; Burd R S; Kurrelmeyer K M; Ratz C A; Dunn D L. (Department of Surgery, University of Minnesota, Minneapolis.) ARCHIVES OF SURGERY, (1994 Feb) 129 (2) 179-80. Journal code: 9716528. ISSN: 0004-0010. Pub. country: United States. Language: English.
AB OBJECTIVE: This study tried to determine whether administration of antilipopolysaccharide (LPS) murine monoclonal **antibody** (mAb) **2A3** to mice was associated with (1) protective capacity during experimental gram-negative bacterial sepsis, and (2) inhibition of tumor necrosis factor alpha (TNF-alpha) secretion in the systemic circulation and at the tissue level during experimental infection. DESIGN: Mice received an initial intravenous injection of either saline or 100 micrograms of anti-LPS mAb **2A3**, and 1 hour later underwent intraperitoneal inoculation of viable Escherichia coli 0111:B4. Mortality

was assessed daily for 7 days. Separate groups of mice were treated similarly and plasma TNF-alpha concentrations were determined from blood samples obtained at 1, 3, 6, 10, and 16 hours after infection by enzyme-linked immunosorbent assay. Concurrently, splenocytes harvested from animals 3, 10, and 16 hours after infection were incubated in culture ex vivo and supernatant TNF-alpha levels were determined. RESULTS: Pretreatment with anti-LPS mAb **2A3** prior to an intraperitoneal challenge of live E coli 0111:B4 was associated with the following: (1) significant protective capacity (100% vs 0% mortality, P < .001); (2) inhibition of plasma TNF-alpha levels 16 hours after infection (1257 +/- 323 pg/mL vs 292 +/- 254 pg/mL, P < .001); and (3) abrogation of TNF-alpha secretion derived from splenic macrophages isolated 16 hours after bacterial challenge (229 +/- 12 pg/mL vs 107 +/- 48 pg/mL, P < .05). CONCLUSIONS: These results strongly support the contention that inhibition of LPS-induced TNF-alpha secretion at both the tissue and systemic levels is a key mechanism by which anti-LPS mAbs provide protection during gram-negative bacterial peritonitis. We believe that in vivo monitoring of macrophage cytokine secretion will be critical for elucidating the precise role of a variety of mediators in the pathogenesis of gram-negative bacterial sepsis.

L8 ANSWER 36 OF 68 MEDLINE on STN DUPLICATE 18

95243800 Document Number: 95243800. PubMed ID: 7537037. Generation of monoclonal **antibodies** that distinguish between mesotheliomas and other tumor of the lung. Narumi K; Chen F A; Bankert R B; Takita H. (Department of Molecular Immunology, New York State Department of Health, Roswell Park Cancer Institute, Buffalo, USA.) NIPPON GEKA HOKAN. ARCHIV FUR JAPANISCHE CHIRURGIE, (1994 Jul 1) 63 (4) 129-38. Journal code: 0421143. ISSN: 0003-9152. Pub. country: Japan. Language: English.

AB The accurate diagnosis of mesothelioma remains difficult despite advances of diagnostic technique. And specific monoclonal **antibody** (McAb) against mesothelioma have not been reported. In an attempt to develop mesothelioma specific McAb(s), spleen cells from a mouse immunized with isolated tumor cells were fused to a drug resistant mouse myeloma cell lines. Over 200 hybridomas were assayed for their preferential reactivity with mesothelioma cell lines or mesothelioma tumor biopsy tissues. Two monoclonal **antibodies 2A3** and 4E1 were identified that bound 6/7 of the mesotheliomas, tested, but did not bind to the majority, 11/13 (for **2A3**) and 12/13 (for 4E1), of other lung tumor types. Based upon western blot analysis of one and two-dimensional gels and upon the distribution pattern of the **antibody** recognized molecule in mesotheliomas and non-mesothelioma lung tumors, **2A3** binds to the cell adhesion molecule CD44. While the specificity of 4E1 has not yet been unequivocally established it appears to recognize a variant form of the CD44 molecule.

L8 ANSWER 37 OF 68 MEDLINE on STN DUPLICATE 19

94006902 Document Number: 94006902. PubMed ID: 8403195. Cytochrome P450 forms in the rodent lung involved in the metabolic activation of food-derived heterocyclic amines. Hellmold H; Overvik E; Stromstedt M; Gustafsson J A. (Department of Medical Nutrition, Karolinska Institute, Huddinge, Sweden.) CARCINOGENESIS, (1993 Sep) 14 (9) 1751-7. Journal code: 8008055. ISSN: 0143-3334. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The metabolic activation of the promutagens 2-amino-3,8-dimethylimidazo[4,5-f]quinoline (IQ), 2-amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx) and 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) by rat and mouse lung microsomes was studied using Salmonella mutagenicity (strain TA98). Lungs from uninduced animals were found to activate all three compounds. A 4-6 fold higher mutagenic activity was obtained with IQ compared to MeIQx and the mutagenic response of PhIP was 1-2 orders of magnitude lower than that of IQ. In order to characterize the forms of P450 in the lung responsible for the metabolic activation of these food mutagens Western blots were performed with microsomes and

partially purified P450 fractions from the lung. Western blots revealed the presence of cytochrome P450 2A, 2B and 4A forms in untreated rats. In the lung CYP 1A1 was only detectable after BNF treatment of rats. The CYP 4A isozymes, which have not previously been described in the rat lung, were further identified after PCR amplification from lung mRNA as 4A2 and 4A8. **Antibody** inhibition studies showed that CYP **2A3** catalyzed a major part (70%) of the metabolic activation of IQ by uninduced rat lung microsomes. The metabolic activation of MeIQx was not influenced by this **antibody**. An **antibody** against CYP 2B isozymes also partially inhibited the activation of IQ by uninduced rat lung microsomes. However, since induction of CYP 2B isozymes in the liver by phenobarbital treatment did not increase the metabolic activation of the heterocyclic amines over controls it is unlikely that the rat lung CYP 2B1 is participating in the activation of heterocyclic amines. The inhibition of the IQ-dependent mutagenicity by the CYP 2B **antibody** is probably due to cross-reaction with CYP **2A3**. Alfa-naphthoflavone (ANF), considered to be a specific inhibitor of CYP 1A isozymes at 10 microM, partly inhibited the activation of IQ (30-40%) and MeIQx (60-80%) by uninduced rat and mouse lung microsomes. Upon pretreatment of rats with BNF, lung microsomes activated MeIQx at a rate that was 2-10-fold higher than control lung microsomes, whereas the increase in EROD activity was approximately 100-fold in the same lung preparations. These results suggest that CYP 1A1 may not be the enzyme responsible for the activation of MeIQx in the control rat despite the inhibition with ANF. It is likely that ANF can inhibit other P450 enzymes in the lung, including CYP **2A3**.(ABSTRACT TRUNCATED AT 400 WORDS)

L8 ANSWER 38 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 20

1993:361667 Document No.: PREV199396047342. Development and characterization of monoclonal **antibodies** recognizing deoxyribonucleoside derivatives. Choi, Eun-Mi. Dep. Chem., Coll. Nat. Sci., Incheon Univ., Incheon 402-749, North Korea. Korean Biochemical Journal, (1993) Vol. 26, No. 2, pp. 118-124.
CODEN: KBCJAK. ISSN: 0368-4881. Language: English.

AB A purine deoxyriboside (6-thiopurine-2'-deoxyriboside, dPu-SH) and a pyrimidine deoxyriboside (4-thio-2'-deoxyuridine, dU-SH) were conjugated to bovine serum albumin (BSA) in the way that deoxyribose rings were exposed by linking C-6 of purine ring and C-4 of pyrimidine ring to the protein, respectively. Monoclonal **antibodies** were produced by using these two conjugates as antigens. Group I monoclonal **antibodies** (1B2, **2A3**, 4D4, and 8B6) from dPu-BSA immunized mouse showed affinity for purine deoxyriboside derivatives with substitution on N-1, C-2, and C-6 but showed no affinity for the derivatives with N-7 and C-8 substitution. Group II monoclonal **antibodies** (3A3, 3A5, 6A2, and 9B1) from dU-BSA immunized mouse showed affinity for pyrimidine deoxyribosides with substitution on C-2, C-4, and C-5. None of the **antibodies** had affinity for base derivatives, deoxyribose, and ribonucleosides. It suggests that these monoclonal **antibodies** may be useful for the study of mechanisms of DNA damage by facilitating isolation of various deoxyribonucleotides excised from damaged DNA.

L8 ANSWER 39 OF 68 CAPLUS COPYRIGHT 2003 ACS on STN

1993:146104 Document No. 118:146104 Preparation of monoclonal **antibody** to aflatoxins for food analysis. Tsunnche, Tsuen (National Science Council, Taiwan). Jpn. Kokai Tokkyo Koho JP 04360695 A2 19921214 Heisei, 8 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1991-126021 19910529.

AB Monoclonal **antibody** (MAb) to aflatoxins, that can be used for detection of aflatoxins B1, B2, G1, and G2 in food, feed, and agricultural products, is provided. The MAb-secreting hybridoma A25-**2A3**-3E6-IE3 is prepd. by fusion of the aflatoxin-immunized BALB/c spleen cells with a mouse myeloma cell P3-NS/1-Ag4-1(NS-1) and selection in the

HAT medium. These MAbs were used for ICELISA.

L8 ANSWER 40 OF 68 MEDLINE on STN DUPLICATE 21

92185558 Document Number: 92185558. PubMed ID: 1545260. Human antiglioma monoclonal **antibodies** from patients with astrocytic tumors. Dan M D; Schlachta C M; Guy J; McKenzie R G; Dorscheid D R; Sandor V A; Villemure J G; Price G B. (Department of Neurology and Neurosurgery, McGill Cancer Centre, McGill University, Montreal, Quebec, Canada.) JOURNAL OF NEUROSURGERY, (1992 Apr) 76 (4) 660-9. Journal code: 0253357. ISSN: 0022-3085. Pub. country: United States. Language: English.

AB The current management of malignant gliomas is unsatisfactory compared to that of other solid tumors; the expected median survival period is less than 1 year with the patient undergoing conventional surgery, radiotherapy, and chemotherapy treatment. Immunological reagents could be a useful adjunct. Human monoclonal **antibodies** derived from patients with astrocytic tumors might recognize subtle antigenic specificities that would differ from those recognized by xenogeneic (murine) systems. Five hybridomas, designated as BT27/1A2, BT27/**2A3**, BT32/A6, BT34/A5, and BT54/B8, were produced from the fusion of peripheral blood lymphocytes of four patients with astrocytic tumors to the human myeloma-like cell line TM-H2-SP2. This cell line has a 46, XX karyotype and is negative for hypoxanthine guanine phosphoribosyltransferase. All five human monoclonal **antibodies** produced 2.4 to 44 micrograms/ml of immunoglobulin M, had a similar but not identical pattern of reactivity against a panel of human tumor cell lines, and failed to react with normal human astrocytes. Labeling of four neuroectodermal tumor explant cultures by BT27/**2A3** was demonstrated by flow cytometry. Karyotyping of three of the five hybridomas demonstrated that two were pseudodiploid (2-3n) and one hypodiploid (less than 2n). The monoclonality of the hybridomas was evaluated by Southern blot analysis of JH gene rearrangements, revealing two types of rearrangements for each hybridoma, both consistent with monoclonality. Preliminary antigen characterization indicated that at least four of the five human monoclonal **antibodies** were directed to cell-surface glycolipids.

L8 ANSWER 41 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 22

1993:80799 Document No.: PREV199395045299. Preparation and characterization of a monoclonal **antibody** against aflatoxins B-1, B-2, G-1 and G-2. Seng, Tsung-Che [Reprint author]; Li, Ishien; Chao, Yung-Hsu. Institute of Botany, Academia Sinica, Nankang, Taipei, Taiwan. Botanical Bulletin of Academia Sinica (Taipei), (1992) Vol. 33, No. 4, pp. 369-374. CODEN: BBASA6. ISSN: 0006-8063. Language: English.

AB By using an indirect enzyme-linked immunosorbent assay (Indirect ELISA), a monoclonal **antibody** (McAb) designed as 1E3 was generated after fusion of mouse (P3-NS1-Ag4-1) myeloma cells with spleen cells isolated from BALB/c mice, which were immunized with aflatoxin B1-BSA conjugated. The McAb has a high affinity for aflatoxins B-1, B-2, G-1, and G-2. Specially, it has the greatest binding efficiency for aflatoxin B-1 based on an indirect competitive ELISA (indirect cELISA). The cross reactivities of the **antibody** with a family of aflatoxin group were 0.44 ng/ml (22 pg/assay), 2.1 ng/ml (105 pg/assay), 3.0 ng/ml (150 pg/assay), 7.3 ng/ml (365 pg/assay), and 1.4 ng/ml (70 pg/assay) for aflatoxins B-1, B-2, G-1, G-2 and total aflatoxins (B-1, B-2, G-1, and G-2), respectively. Aflatoxins M-1, M-2, B-2a, G-2a, R-0, P-1, Q-1, and sterigmatocystin showed almost no cross-reaction with the **antibody**. The **antibody** producing cell line (A25-**2A3**-3E6-1E3), which has been maintained for more than three years, secreted murine IgG class immunoglobulin and was characterized as IgG-1 with Lambda light chains. The potential to use the **antibody** to detect the four natural occurrence of aflatoxins (B-1, B-2, G-1, and G-2) in foods or agricultural products was stressed.

L8 ANSWER 42 OF 68 MEDLINE on STN DUPLICATE 23
93020366 Document Number: 93020366. PubMed ID: 1403797. Human anti-cytochrome P450 **antibodies** in aromatic anticonvulsant-induced hypersensitivity reactions. Leeder J S; Riley R J; Cook V A; Spielberg S P. (Department of Pediatrics, Hospital for Sick Children, Toronto, Ontario, Canada.) JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1992 Oct) 263 (1) 360-7. Journal code: 0376362. ISSN: 0022-3565. Pub. country: United States. Language: English.

AB Aromatic anticonvulsants such as phenytoin, phenobarbital and carbamazepine are associated with a hypersensitivity syndrome (fever, rash lymphadenopathy, hepatitis) suggestive of an immune component. We have identified immunoglobulin G **antibodies** in the sera of nine affected patients which recognize a 53-kD protein which is constitutively expressed and PB inducible in rat liver microsomes. No such reactivity was observed in sera from healthy controls, patients on chronic phenytoin therapy without toxicity or patients with hepatic failure not receiving anticonvulsants. Using highly purified rat hepatic cytochrome P450, P450 3A1 was identified as the major antigenic species, whereas less intense reactivity was noted with P450 2C11. P450 2C6 and 3A2 were minor antigens in some patients. In all patients, the apparent constitutive and phenobarbital-inducible expression of the antigen was a composite effect of **antibodies** reacting with at least two isozymes, one of which was constitutively expressed and the other PB inducible. In human liver, a 53-kD antigen was expressed to a greater extent in microsomes from a patient with a fatal hepatotoxic reaction to phenytoin compared to microsomes from normal liver or from a sulfonamide hepatitis patient. Western blotting with microsomes prepared from lymphoblastoid cell lines transfected with different human hepatic cytochromes P450 failed to identify P450s 1A1, 1A2, **2A3**, 2B6, 2C9, 2D6, 2E1, 3A4 or epoxide hydrolase as the target antigen. Identification of the antigen will be important in understanding the relationship between drug metabolism and the subsequent immune response in the pathogenesis of these rare but severe forms of drug toxicity.

L8 ANSWER 43 OF 68 MEDLINE on STN DUPLICATE 24
92319755 Document Number: 92319755. PubMed ID: 1620688. Purification and characterization of kallikrein-like serine proteases from rat submandibular glands. Bedi G S. (Department of Oral Biology, State University of New York, Buffalo 14214.) PREPARATIVE BIOCHEMISTRY, (1992 Mar) 22 (1) 67-81. Journal code: 1276634. ISSN: 0032-7484. Pub. country: United States. Language: English.

AB The purification and characterization of kallikrein-like proteases from rat submandibular glands is described. The proteolytic activity of each fraction during purification was monitored on the synthetic substrate N-alpha-tosyl-L-arginine methyl ester (TAME). The purification scheme involved ammonium sulfate precipitation, chromatography on columns of DEAE-Sepharose and Sephadex G-100 and chromatofocusing. Three TAME-hydrolytic activity peaks were eluted from DEAE-Sepharose as unbound fraction (Pool 1), at 125 mM NaCl (Pool 2) and at 250 mM NaCl concentration (Pool 4). Pool 1 further resolved into two protease fractions (1A1 and 1A2), pool 2 into three protease fractions (2A1, 2A2 and **2A3**) and pool 4 gave a single major protease peak (4A1) by chromatofocusing on PBE-94. Protease pools 2A2, **2A3**, and 4A1 each gave a single band on SDS-polyacrylamide gel electrophoresis with an estimated molecular weight of 34 kDa, 46 kDa and 46 kDa respectively. Pools 1A1, 1A2, 2A1 and 2a2 gave a single precipitin line with anti-rat glandular kallikrein **antibodies**. **2A3** and 4A1 did not react with these **antibodies**. Synthetic substrates DL-val-leu-arg-pNA and Bz-pro-phe-arg-pNA, specific for kallikrein-like proteases, were hydrolyzed preferentially by **2A3** and 4A1 but were poor substrates for 1A1, 1A2, 2A1 and 2A2.

L8 ANSWER 44 OF 68 MEDLINE on STN DUPLICATE 25
92072332 Document Number: 92072332. PubMed ID: 1961012. Resistance of

myeloid leukaemia cell lines to ricin A-chain immunotoxins. Engert A; Brown A; Thorpe P. (Drug Targeting Laboratory, Imperial Cancer Research Fund, London, U.K.) LEUKEMIA RESEARCH, (1991) 15 (11) 1079-86. Journal code: 7706787. ISSN: 0145-2126. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Nineteen monoclonal **antibodies** that recognize antigens on myeloid leukaemia cells were screened upon HL60, KG1, U937 and K562 cells for their ability to form effective ricin A-chain immunotoxins. The screening was performed using an indirect assay in which the cells were treated firstly with the test **antibody** and then with a Fab' immunotoxin directed against mouse immunoglobulin. Only two **antibodies**, MEM75 and 120-**2A3**, both directed against the transferrin receptor (TfR) were predicted to form immunotoxins that would inhibit protein synthesis by the cells by 50% at a concentration (IC50) of 10(-8) M or less. This prediction was subsequently confirmed using several of the **antibodies** directly conjugated to ricin A-chain. By contrast, the same immunotoxins were highly toxic to non-myeloid cells which shared the target antigens. A comparison was made between the rates of endocytosis and degradation by HL60 cells of an anti-TfR immunotoxin 120-**2A3**.dgA, that was effective at killing myeloid cells, and a CD33 immunotoxin, p67-7.dgA, that bound to myeloid cells but did not kill them. The difference in potency of the two immunotoxins on HL60 cells was not due to deficient uptake of p67-7.dgA but was probably due to the more rapid intracellular degradation of p67-7.dgA. Fast and effective degradation in lysosomes, if a general finding, could explain the poor susceptibility of myeloid cells to ricin A-chain immunotoxins.

L8 ANSWER 45 OF 68 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

91:681180 The Genuine Article (R) Number: GU892. RESISTANCE OF MYELOID-LEUKEMIA CELL-LINES TO RICIN A-CHAIN IMMUNOTOXINS. ENGERT A (Reprint); BROWN A; THORPE P. UNIV COLOGNE, MED KLIN 1, W-5000 COLOGNE 41, GERMANY (Reprint); IMPERIAL CANC RES FUND, DRUG TARGETING LAB, LONDON WC2A 3PX, ENGLAND. LEUKEMIA RESEARCH (1991) Vol. 15, No. 11, pp. 1079-1086. Pub. country: GERMANY; ENGLAND. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Nineteen monoclonal **antibodies** that recognize antigens on myeloid leukaemia cells were screened upon HL60, KG1, U937 and K562 cells for their ability to form effective ricin A-chain immunotoxins. The screening was performed using an indirect assay in which the cells were treated firstly with the test **antibody** and then with a Fab' immunotoxin directed against mouse immunoglobulin. Only two **antibodies**, MEM75 and 120-**2A3**, both directed against the transferrin receptor (TfR) were predicted to form immunotoxins that would inhibit protein synthesis by the cells by 50% at a concentration (IC50) of 10(-8) M or less. This prediction was subsequently confirmed using several of the **antibodies** directly conjugated to ricin A-chain. By contrast, the same immunotoxins were highly toxic to non-myeloid cells which shared the target antigens. A comparison was made between the rates of endocytosis and degradation by HL60 cells of an anti-TfR immunotoxin 120-**2A3**.dgA, that was effective at killing myeloid cells, and a CD33 immunotoxin, p67-7.dgA, that bound to myeloid cells but did not kill them. The difference in potency of the two immunotoxins on HL60 cells was not due to deficient uptake of p67-7.dgA but was probably due to the more rapid intracellular degradation of p67-7.dgA. Fast and effective degradation in lysosomes, if a general finding, could explain the poor susceptibility of myeloid cells to ricin A-chain immunotoxins.

L8 ANSWER 46 OF 68 MEDLINE on STN DUPLICATE 26

91243200 Document Number: 91243200. PubMed ID: 1674673. Interactions between CD3 and Thy1 T cell activation pathways: blockade of CD3-mediated T lymphocyte activation induced by immobilized anti-Thy1 **antibodies**. Bellio M; Leal L M; Scharfstein J; Dos Reis G A. (Carlos Chagas Filho Institute of Biophysics, Federal University of Rio de Janeiro, Brazil.) CELLULAR IMMUNOLOGY, (1991 Jul) 135 (2) 534-40.

Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

AB Resting murine T cell activation induced by either CD3 complexes or Thy1 molecules was investigated in vitro, using surface-bound anti-CD3 mAb as the stimulus. One mitogenic anti-Thy 1 mAb (G7) lost mitogenicity when presented to T cells immobilized on a plastic surface, even in the presence of phorbol ester. Moreover, T cell activation induced by immobilized anti-CD3 was potently blocked by coimmobilized anti-Thy 1 mAb. Nonmitogenic anti-Thy 1 mAb also blocked CD3-induced activation when coimmobilized with anti-CD3. Control experiments showed that anti-Thy 1 specifically blocked T cell activation, even in the presence of measurable and functional concentrations of plastic-bound anti-CD3. Coimmobilized anti-Thy 1 potently blocked IL2 secretion stimulated by anti-CD3. Addition of exogenous rIL2 completely prevented anti-Thy 1-mediated blockade. On the other hand, while completely blocking T cell proliferation, immobilized anti-Thy 1 only partially blocked secretion of IL3-like activity by the T cells. One IgM anti-Thy 1 mAb (**2A3**) induced secretion of IL3-like activity by T cells when immobilized in the absence of bound anti-CD3. These results indicate that extensive aggregation of Thy 1 molecules delivers a potent negative signal which antagonizes CD3-mediated T cell activation and growth.

L8 ANSWER 47 OF 68 MEDLINE on STN DUPLICATE 27

91300193 Document Number: 91300193. PubMed ID: 2070147. Prophylaxis of graft-versus-host disease by administration of the murine anti-IL-2 receptor **antibody 2A3**. Anasetti C; Martin P J; Storb R; Appelbaum F R; Beatty P G; Calori E; Davis J; Doney K; Reichert T; Stewart P; +. (Fred Hutchinson Cancer Research Center, Seattle, WA 98104.) BONE MARROW TRANSPLANTATION, (1991 May) 7 (5) 375-81. Journal code: 8702459. ISSN: 0268-3369. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The efficacy of murine monoclonal IgG1 **antibody 2A3** specific for the 55 kD chain of the human IL-2 receptor (CD25) was evaluated for prophylaxis of acute GVHD in patients with advanced leukemia transplanted with unmodified bone marrow from related HLA-haploidentical donors incompatible for two or three HLA loci of the nonshared haplotype. As GVHD prophylaxis, 36 patients (control) received standard cyclosporine and methotrexate (C + M) whereas 11 patients (study) received C + M plus **antibody 2A3**, 1.0 mg/kg on day -1, and 0.5 mg/kg daily from day 0 through day +19. **Antibody** administration was not associated with appreciable toxicity and did not adversely affect engraftment. During treatment, circulating CD25+ cells appeared saturated by the infused **antibody**. Patients receiving **antibody 2A3** tolerated more cyclosporine than controls (p less than 0.001) with lower increase of serum creatinine (p less than 0.05) during the first month. Seven of 10 (70%) evaluable study patients developed acute GVHD of grade II-IV with onset at a median of 20 days compared to 27 of 31 (87%) control patients with onset at a median of 13 days (p = 0.11). Trough serum levels of **antibody 2A3** ranged from 7.2 to 68.8 mg/l, and lower values correlated with occurrence of acute GVHD. A human anti-mouse immunoglobulin **antibody** response was detected in four patients but was not associated with lower levels of **antibody 2A3** in the serum. Two study patients and two controls have survived more than 1 year (p = 0.92). These findings suggest that administration of **antibody 2A3** suppressed and delayed activation of alloantigen-specific T cells but did not result in their elimination.

L8 ANSWER 48 OF 68 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

91:307992 The Genuine Article (R) Number: FN363. PROPHYLAXIS OF GRAFT-VERSUS-HOST DISEASE BY ADMINISTRATION OF THE MURINE ANTI-IL-2 RECEPTOR **ANTIBODY-2A3**. ANASETTI C (Reprint); MARTIN P J; STORB R; APPELBAUM F R; BEATTY P G; CALORI E; DAVIS J; DONEY K; REICHERT T; STEWART P; SULLIVAN K M; THOMAS E D; WITHERSPOON R P; HANSEN J

A. FRED HUTCHINSON CANC RES CTR, 1124 COLUMBIA ST, SEATTLE, WA, 98104 (Reprint); BECTON DICKINSON MONOCLONAL CTR INC, SAN JOSE, CA, 00000; UNIV WASHINGTON, DEPT MED, DIV ONCOL, SEATTLE, WA, 98195. BONE MARROW TRANSPLANTATION (1991) Vol. 7, No. 5, pp. 375-381. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The efficacy of murine monoclonal IgG1 **antibody 2A3** specific for the 55 kD chain of the human IL-2 receptor (CD25) was evaluated for prophylaxis of acute GVHD in patients with advanced leukemia transplanted with unmodified bone marrow from related HLA-haploidentical donors incompatible for two or three HLA loci of the non-shared haplotype. As GVHD prophylaxis, 36 patients (control) received standard cyclosporine and methotrexate (C + M) whereas 11 patients (study) received C + M plus **antibody 2A3**, 1.0 mg/kg on day -1, and 0.5 mg/kg daily from day 0 through day +19. **Antibody** administration was not associated with appreciable toxicity and did not adversely affect engraftment. During treatment, circulating CD25 + cells appeared saturated by the infused **antibody**. Patients receiving **antibody 2A3** tolerated more cyclosporine than controls ($p < 0.001$) with lower increase of serum creatinine ($p < 0.05$) during the first month. Seven of 10 (70%) evaluable study patients developed acute GVHD of grade II-IV with onset at a median of 20 days compared to 27 of 31 (87%) control patients with onset at a median of 13 days ($p = 0.11$). Trough serum levels of **antibody 2A3** ranged from 7.2 to 68.8 mg/l, and lower values correlated with occurrence of acute GVHD. A human anti-mouse immunoglobulin **antibody** response was detected in four patients but was not associated with lower levels of **antibody 2A3** in the serum. Two study patients and two controls have survived more than 1 year ($p = 0.92$). These findings suggest that administration of **antibody 2A3** suppressed and delayed activation of alloantigen-specific T cells but did not result in their elimination.

L8 ANSWER 49 OF 68 MEDLINE on STN DUPLICATE 28
91134148 Document Number: 91134148. PubMed ID: 1899725. Monoclonal **antibodies** identify micronemes and a new population of cytoplasmic granules cross-reacting with micronemes of cystozoites of Sarcocystis muris. Entzeroth R; Konig A; Dubremetz J F. (Zoologisches Institut, Bonn, Federal Republic of Germany.) PARASITOLOGY RESEARCH, (1991) 77 (1) 59-64. Journal code: 8703571. ISSN: 0932-0113. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Micronemes of cystozoites of Sarcocystis muris were isolated after subcellular fractionation and used for immunization of BALB/C mice. After spleen cells of immunized mice were fused with SP20 myeloma cells, ten different monoclonal **antibodies** (mAbs) were isolated. These **antibodies** reacted with antigens whose molecular weight ranged from 16 to greater than 90 kDa. Six mAbs recognized granules of 150-400 nm that were located in the vicinity of the Golgi complex but were not identical with dense granules. Two mAbs (**2A3**, 3A8) were specific for micronemes of cystozoites as demonstrated by immunoelectron microscopy. However, these **antibodies** also recognized the population of granules near the Golgi complex. Cross-reactivity between micronemes and a dense granule population has not previously been reported. Host cells that had been contacted by cystozoites showed patchy fluorescence when probed with mAb **2A3**. This suggests that microneme antigens could be transferred to the host-cell surface during parasite-host cell interactions.

L8 ANSWER 50 OF 68 CAPLUS COPYRIGHT 2003 ACS on STN
1991:677459 Document No. 115:277459 Effect of cross-linking of lymphocyte surface antigens on the levels of intracellular calcium. Lozano, F.; Places, L.; Alberola-Ila, J.; Vives, J. (Serv. Immunol., Hosp. Clin. Provincial, Barcelona, 08036, Spain). Inmunologia, 10(2), 35-42 (Spanish) 1991. CODEN: INMNEC. ISSN: 0212-5765.

AB Monoclonal **antibodies** (mAbs) were studied with respect to their ability to mobilize intracellular calcium. For this purpose, peripheral blood mononuclear cells were incubated with the Indo-1/AM dye and then analyzed for flow cytometry after the addn. of different mAbs. Except for mAb 33-**2A3** (anti-CD3), none of the tested mAbs was able by itself to induce increments in the base levels of intracytoplasmic Ca++. On the contrary, the addn. of a polyclonal antiserum against mouse Igs to favor the crosslinking of the surface mols. was able to induce different effects on the levels of cytoplasmic Ca++. The crosslinking of the mol. detected by mAb anti-CD3 did not induce increments significantly higher in respect to that obtained by itself. No effects were obsd. after the crosslinking of the surface mols. detected by mAbs specific for CD4, CD5, CD7, CD8, CD14, CD18, CD20, CD25, CD26, CD44, CD45, CD71, CD76, and HLA class I and II. Only the crosslinking of the mols. recognized by mAbs specific for CD2 and CD43 induced significant increments in the base levels of intracytoplasmic Ca++. Meanwhile the increment mediated by CD2 was very important and persistent; the one induced through CD43 was lower not only in magnitude but also in duration. The increment in the intracytoplasmic Ca++ mediated by anti-CD43 mAb was clearly dependent on the entry of extracellular Ca++, for it was inhibited by the presence of EGTA. The increment in the intracytoplasmic Ca++ induced by anti-CD43 mAb was dependent on the presence of adherent cells and was inhibited by preincubation for short periods of time (5 min to 1 h) with high doses of the phorbol ester deriv. PMA (100 ng/mL). The mobilization of Ca++ mediated by anti-CD43 mAb was blocked by incubation of the cells overnight with anti-CD43 mAb, but not when cells were incubated with PMA (100 ng/mL) or with anti-CD3 mAb, indicating that the phenomenon was specific for CD43 and was mediated through the CD3/T cell receptor complex.

L8 ANSWER 51 OF 68 MEDLINE on STN DUPLICATE 29

90308284 Document Number: 90308284. PubMed ID: 1973183.

Alloantigen-specific T suppressor-inducer and T suppressor-effector cells can be activated despite blocking the IL-2 receptor. Tan P; Anasetti C; Martin P J; Hansen J A. (Division of Clinical Research, Fred Hutchinson Cancer Research Center, Seattle 98104.) JOURNAL OF IMMUNOLOGY, (1990 Jul 15) 145 (2) 485-8. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB To determine IL-2 requirement for activation of suppressor cells, PBMC were primed in one-way MLR in the presence of 10 micrograms/ml anti-IL-2R beta-chain **antibody 2A3** (CD25) or control **antibody**, then irradiated and added as regulators in a fresh MLR. Cells primed in the presence of **antibody 2A3** suppressed the proliferative response to fresh autologous lymphocytes to specific alloantigen but had no effect on the response to cells from third party donors. Priming in the presence of an **antibody** of irrelevant specificity induced only limited suppressor activity. Activated suppressor cells did not show cytolytic activity specific for the stimulators when tested at the time of the suppressor cell assay. To identify the subset(s) responsible for suppression, cells primed in the presence of **antibody 2A3** were separated into CD4+/CD45RA+, CD4+/CD45RA-, and CD8+ subsets, which were irradiated and then tested. The suppressive activity was found predominantly in the CD4+/CD45RA+ subset, whereas CD8+ cells had some activity and CD4+/CD45RA- cells had none. No subset suppressed the response of autologous cells to third-party cells. When primed CD4+/CD45RA+ cells were cocultured with fresh autologous lymphocytes depleted of CD8+ cells, no suppression was observed, indicating that, although the CD4+/CD45RA+ cells can function as inducers of suppressors, they cannot function as suppressor-effectors. Conversely, CD8+ cells activated in MLR in the presence of **2A3** caused suppression, regardless of whether the fresh autologous responder population contained CD8+ cells. CD4+/CD45RA+ and CD8+ subsets isolated after priming in the presence of **2A3** also demonstrated Ag-specific suppression in the generation of cytotoxic T lymphocytes whereas CD4+/CD45RA- cells had no activity. Our data are consistent with

the model that suppression of alloreactivity requires the cooperation of two types of cells, a CD4+/CD45RA+ suppressor-inducer and a CD8+ suppressor-effector population. Activated Tsi and fresh Tse or activated Tse alone can suppress lymphocyte proliferation and generation of CTL in response to specific Ag. Activation of Ag-specific T suppressor-inducer and T suppressor-effector cells appears to be relatively IL-2 independent and presumably require one or more other growth factors.

L8 ANSWER 52 OF 68 MEDLINE on STN DUPLICATE 30
91273053 Document Number: 91273053. PubMed ID: 2097902. [Production and characterization of a high affinity monoclonal **antibody** with digoxin and digitoxin specificity]. Produktion und Charakterisierung eines hochaffinen monoklonalen Antikorpers mit Digoxin- und Digitoxin-Spezifitat. Simon H U; Hubl W; Muller W D; Wolf I; Schlenvoigt G; Jager L. (Institut fur Klinische Immunologie, Friedrich-Schiller-Universitat Jena.) ALLERGIE UND IMMUNOLOGIE, (1990) 36 (4) 343-50. Journal code: 0314702. ISSN: 0323-4398. Pub. country: GERMANY: Germany, Federal Republic of. Language: German.
AB A monoclonal **antibody** with a high affinity for digoxin (KA = 5.5 x 10(10) M-1) and digitoxin KA = 5.0 x 10(10) M-1) was produced by somatic cell fusion. This **antibody**, designated **2A3**, displayed little cross reactivity with other glucosides and no cross reactivity with endogenous steroids. It was shown that **2A3** is a suitable tool in an enzyme immunoassay for digoxin and digitoxin.

L8 ANSWER 53 OF 68 MEDLINE on STN DUPLICATE 31
91355705 Document Number: 91355705. PubMed ID: 1715776. A human monoclonal autoantibody specific for human platelet glycoprotein IIb (integrin alpha IIb) heavy chain. Kunicki T J; Furihata K; Kekomaki R; Scott J P; Nugent D J. (Blood Center of Southeastern Wisconsin, Inc., Milwaukee 53233.) HUMAN ANTIBODIES AND HYBRIDOMAS, (1990) 1 (2) 83-95. Journal code: 9014461. ISSN: 0956-960X. Pub. country: United States. Language: English.
AB Splenocytes from a patient with chronic, immune-mediated thrombocytopenic purpura (ITP) were transformed with Epstein-Barr virus. A stable lymphoblastoid cell line (LCL) derived from this transformation (**2A3**) produces IgM **antibody** reactive with platelet glycoprotein IIb. **2A3** was fused to the 6-thioguanine-resistant ouabain-resistant, murine-human heteromyeloma cell line, F6. The resultant heterohybridomas were selected by growth in medium containing hypoxanthine/aminopterin/thymidine and ouabain. One hybridoma line, 2E7, produces high levels of IgM **antibody** (2 to 4 micrograms IgM/ml/24 hr/10(5) cells) reactive with glycoprotein IIb. 2E7 has been repeatedly subcloned by limiting dilution and has been maintained in continuous culture for 26 months. 2E7 binds to human platelets but not endothelial cells, as determined by flow cytometry, and does not react with platelets of patients with Glanzmann's thrombasthenia that lack IIb-IIIa. The epitope recognized by 2E7 is likely to be a contiguous peptide sequence since the **antibody** binds to the IIb heavy chain in immunoblot assays of denatured, reduced platelet protein. Treatment of intact platelets or purified IIb-IIIa with papain or chymotrypsin, but not SV8 protease, destroys the epitope. Thus, the 2E7 epitope may be at or very close to a site on IIb that is cleaved by these proteases. The expression of the 2E7 epitope is significantly affected by the presence of divalent cations. Treatment of intact platelets with EDTA at 37 degrees C results in a three-to four-fold increase in the number of 2E7 molecules bound per platelet and an eight-fold increase in the affinity of the **antibody**. The binding of 2E7 to normal platelets does not inhibit any of the functions attributed to IIb-IIIa, such as fibrinogen-dependent platelet aggregation or clot retraction. 2E7 represents the first human monoclonal **antibody** reported to recognize an epitope on platelet glycoprotein IIb. The epitope is unique to IIb and not shared by other integrin alpha subunits.

L8 ANSWER 54 OF 68 MEDLINE on STN DUPLICATE 32
90179039 Document Number: 90179039. PubMed ID: 2155572. ACTH adrenal cell bioassay: improved sensitivity (12 ng/L) achieved by immunoextraction of ACTH from human plasma by a monoclonal **antibody**. Mitchell R; Lambert A; Crosby S R; White A; Robertson W R. (Department of Clinical Biochemistry (Medicine), University of Manchester, Hope Hospital, Salford, UK.) ANNALS OF CLINICAL BIOCHEMISTRY, (1990 Jan) 27 (Pt 1) 59-64. Journal code: 0324055. ISSN: 0004-5632. Pub. country: ENGLAND: United Kingdom. Language: English.

AB We have previously reported a bioassay for human plasma ACTH based upon trypsin dispersed guinea-pig adrenal cells which was sensitive to 100 ng/L ACTH in unextracted human plasma when measured against human pituitary ACTH (1-39) standard 74/555. We now present a bioassay of increased sensitivity (12 ng/L) which incorporates three major changes. The trypsin/trypsin inhibitor step in the cell dispersion protocol has been replaced with collagenase, donor calf serum (3%) has been incorporated into the standard curve and ACTH has been extracted from human plasma and dilutions of standard hormone by a sephacryl bound monoclonal **antibody** (**2A3**) directed towards the 25-39 sequence. The extracted standard curve has a detection limit of 6 ng/L and the cells can tolerate up to 50% plasma equivalent concentration. Thus, the improved assay has a detection limit of 12 ng/L ACTH in plasma. The assay can now measure bioactive plasma ACTH levels reliably in the normal range.

L8 ANSWER 55 OF 68 MEDLINE on STN DUPLICATE 33
90312636 Document Number: 90312636. PubMed ID: 2368150. A phase I-II study evaluating the murine anti-IL-2 receptor **antibody** **2A3** for treatment of acute graft-versus-host disease. Anasetti C; Martin P J; Hansen J A; Appelbaum F R; Beatty P G; Doney K; Harkonen S; Jackson A; Reichert T; Stewart P; +. (Department of Medicine, Fred Hutchinson Cancer Research Center, University of Washington, Seattle 98104.) TRANSPLANTATION, (1990 Jul) 50 (1) 49-54. Journal code: 0132144. ISSN: 0041-1337. Pub. country: United States. Language: English.

AB A murine IgG1 **antibody** specific for the IL-2-binding site on the human lymphocyte IL-2 receptor beta chain (CD25) was evaluated in 11 patients who developed acute graft-versus-host disease following allogeneic marrow transplantation. All patients had received cyclosporine and methotrexate for prophylaxis of GVHD, either alone (4 cases), or in combination with antithymocyte globulin (4 cases) or with prednisone (3 cases). Patients had developed GVHD at 7-53 days (median 12) after transplantation and had failed treatment with corticosteroids for 3-44 days (median 19). Residual GVHD was of grade II severity in 4 patients, grade III in 5 patients, and grade IV in 2 patients. Sequential patients received monoclonal **antibody** in escalating doses from 0.1 mg/kg/day to 1.0 mg/kg/day for 7 days. Side effects were fever, respiratory distress, hypertension, hypotension, and chills occurring in 11 of 72 (14%) **antibody** infusions. Trough **antibody** levels greater than 6 micrograms/ml were achieved in patients treated with 0.5 or 1.0 mg/kg/day. Four of eight evaluable patients had an IgM **antibody** response, and one had an IgG response to the murine immunoglobulin. Clinical response of GVHD was evaluated in 10 patients who received the entire course of the **antibody** treatment. Among 7 patients treated within 40 days from transplantation, one patient had a complete response in the skin as the only involved organ, and 3 patients had a partial response, 2 in the skin and one in the gastrointestinal tract. No responses were achieved with liver disease at anytime or in any organ in patients treated beyond 40 days after transplantation. Since administration of this **antibody** was well tolerated and some efficacy was observed in patients with acute GVHD treated early after transplantation, there is a rationale for testing this **antibody** as an agent for prophylaxis of GVHD.

L8 ANSWER 56 OF 68 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
90:390683 The Genuine Article (R) Number: DN689. A PHASE-I PHASE-II STUDY

EVALUATING THE MURINE ANTI-IL-2 RECEPTOR **ANTIBODY-2A3** FOR TREATMENT OF ACUTE GRAFT-VERSUS-HOST DISEASE. ANASETTI C (Reprint); MARTIN P J; HANSEN J A; APPELBAUM F R; BEATTY P G; DONEY K; HARKONEN S; JACKSON A; REICHERT T; STEWART P; STORB R; SULLIVAN K M; THOMAS E D; WARNER N; WITHERSPOON R P. UNIV WASHINGTON, FRED HUTCHINSON CANC RES CTR, DEPT MED, DIV ONCOL, 1124 COLUMBIA ST, SEATTLE, WA, 98104 (Reprint); BECTON DICKINSON MONOCLONAL CTR INC, SAN JOSE, CA, 95131. TRANSPLANTATION (1990) Vol. 50, No. 1, pp. 49-54. Pub. country: USA. Language: ENGLISH.

L8 ANSWER 57 OF 68 MEDLINE on STN DUPLICATE 34

89356528 Document Number: 89356528. PubMed ID: 2767007. Monoclonal **antibodies** specific for antigens expressed by rat type II alveolar epithelial and nonciliated bronchiolar cells. Miller Y E; Walker S R; Spencer J S; Kubo R T; Mason R J. (Department of Medicine, Denver Veterans Administration Medical Center, CO 80220.) EXPERIMENTAL LUNG RESEARCH, (1989 Jul) 15 (4) 635-49. Journal code: 8004944. ISSN: 0190-2148. Pub. country: United States. Language: English.

AB Markers specific for various lung cells are useful for studies of cellular differentiation and function. We have produced monoclonal **antibodies** that bind to isolated rat type II alveolar epithelial cells in an ELISA. Two such **antibodies**, 2C1 and 3F9, specifically labeled type II cells and nonciliated bronchiolar cells by indirect immunofluorescence of rat lung. A third **antibody**, **2A3**, recognized isolated type II cells by ELISA and immunofluorescence, but did not bind to sections of whole lung. Further immunofluorescence studies on adult rat tissue showed that neither 2C1 nor 3F9 labeled other lung cells or cells in kidney, small intestine, brain, or trachea. The antigen or antigens recognized by 2C1 and 3F9 was not detectable at day 15 of fetal lung gestation but was detectable by day 21. Immunofluorescence studies carried out on 0.5-microns frozen sections of lung tissue demonstrated that both 2C1 and 3F9 bound to cell surface antigens, which are expressed in a highly polarized fashion on the luminal surface of the alveolus and bronchiole. The rat cell line, L2, which displays some similarities to type II cells, did not display positive immunofluorescence to **2A3**, 2C1, or 3F9. The **antibodies** 2C1 and 3F9 are distinct from and apparently more specific than previously described monoclonal **antibodies** raised to rat type II cells. Alveolar type II and nonciliated bronchiolar cells share several common features. Both cell types contain the surfactant apoprotein SP-A, proliferate in response to lung injury, develop in the late stages of gestation, take up and catabolize platelet-activating factor, contain high levels of cytochrome P-450, and can be induced to form tumors in response to chemical carcinogens. The recognition of highly specific surface antigen(s) on both nonciliated bronchiolar cells and type II cells demonstrates yet another characteristic shared by the two cell types.

L8 ANSWER 58 OF 68 MEDLINE on STN DUPLICATE 35

90012834 Document Number: 90012834. PubMed ID: 2796047. The clonality and activation of T-cells in sarcoidosis. Konishi K. NIHON KYOBU SHIKKAN GAKKAI ZASSHI. JAPANESE JOURNAL OF THORACIC DISEASES, (1989 Apr) 27 (4) 413-7. Journal code: 7505737. ISSN: 0301-1542. Pub. country: Japan. Language: Japanese.

AB Current concepts of the pathogenesis of sarcoidosis suggest that the expanded numbers of activated T-helper/inducer cells at sites of disease activity result, at least in part, from their proliferation in the local milieu. Normal clonal proliferation of T-cells involves activation and expression of the interleukin-2 receptor (IL-2R) gene; transcription products of which (IL-2R mRNA) are relatively long-lived. We have therefore investigated the hypothesis that sarcoid lung and blood T-cells may contain IL-2R mRNA transcripts and express functional surface IL-2R, because they are activated elsewhere. Northern analysis using a 32P-labeled cDNA probe for the IL-2R alpha chain demonstrated that blood T-cells from patients with active sarcoidosis, but not from normal subjects express 3.5 kb and 1.5 kb IL-2R mRNA transcripts, identical to

the observation when normal T-cells are activated in vitro. Consistent with this, using flow cytometry and a monoclonal **antibody** directed against the IL-2R alpha-chain protein (**2A3**), significant levels of IL-2R protein were observed on the surface of blood T-cells from active sarcoidosis patients but rarely on blood T-cells of normals. Importantly, when the sarcoid blood T-cells were exposed to IL-2 in vitro, they proliferated at a rate greater than did normal blood T-cells under the same conditions, suggesting that the IL-2R spontaneously expressed by sarcoid blood T-cells were functionally active. When placed in the context of the known compartmentalization of spontaneously interleukin-2 production and T-cell proliferation at sites of disease in active pulmonary sarcoidosis, it is likely that these IL-2R positive blood T-cells would have a proliferative advantage if they travel to sites of active sarcoidosis such as the lower respiratory tract.

L8 ANSWER 59 OF 68 MEDLINE on STN DUPLICATE 36

91257910 Document Number: 91257910. PubMed ID: 3154924. Expression of functional human interleukin-2 receptors in murine interleukin-3-dependent cells. Watson J D; Leung E; Eszes M; Le Gros G S; Prestidge R L; Booth R J; Overell R A; Gillis S. (Department of Immunobiology, School of Medicine, University of Auckland, New Zealand.) IMMUNOLOGY AND CELL BIOLOGY, (1988 Aug) 66 (Pt 4) 319-30. Journal code: 8706300. ISSN: 0818-9641. Pub. country: Australia. Language: English.

AB A murine recombinant retrovirus containing the cDNA encoding the human p55 interleukin-2 (IL2)-binding protein was used to insert this gene into a murine interleukin-3 (IL3)-dependent cell line, FD.C/1. Virus-infected cells, maintained in medium supplemented with IL3, expressed human p55 on the cell surface and readily adapted to growth using human IL2. In the presence of human IL2, the synthesis of the endogenous murine p55 binding protein was induced in FD.C/1 cells, making it difficult to determine whether the human p55 protein was actively involved in the process of growth signal transduction. A cloned cell line, FD.huIL2R-2, was identified which grew in the presence of human IL2 but which had lost the ability to synthesize murine p55 protein. Growth of this clone was inhibited by the monoclonal **antibody 2A3** which specifically blocked binding of human IL2 to the human p55 binding protein. Analysis of restriction enzyme digests of FD.huIL2R-2 cell DNA revealed that a rearrangement of a murine p55 gene had occurred, implying that virus infection had resulted in the integration of retroviral DNA at a site close to or within a murine p55 gene. If IL2 signal transduction involves binding to a surface heterodimeric receptor for IL2, it is argued that FD.huIL2R-2 cells contain an IL2 receptor complex of murine p70 and human p55 IL2-binding proteins. Alternatively, it is possible that integration of human p55 DNA into a site close to a murine p55 gene may lead to a hybrid p55 IL2-binding protein. If FD.huIL2R-2 cells express murine p70 IL2-binding protein as part of the receptor complex, the inability of cells to grow in murine IL2 implies that IL2 binding to p70 protein alone is insufficient for a growth signal in these cells. FD.huIL2R-2 cells grow at rates similar in IL3- or human IL2-dependent states. It is likely therefore that the biochemical pathways that control each of these lymphokine-dependent growth states are very similar.

L8 ANSWER 60 OF 68 MEDLINE on STN DUPLICATE 37

88027693 Document Number: 88027693. PubMed ID: 2822290. Measurement of corticotropin in unextracted plasma: comparison of a time-resolved immunofluorometric assay and an immunoradiometric assay, with use of the same monoclonal **antibodies**. Dobson S; White A; Hoadley M; Lovgren T; Ratcliffe J. (Department of Chemical Pathology, University of Manchester, Hope Hospital, Salford, U.K.) CLINICAL CHEMISTRY, (1987 Oct) 33 (10) 1747-51. Journal code: 9421549. ISSN: 0009-9147. Pub. country: United States. Language: English.

AB We describe a time-resolved immunofluorometric assay (IFMA) for corticotropin in unextracted human plasma, based on the use of two monoclonal **antibodies**: europium-labeled **antibody** 1A12

and **antibody 2A3** coated onto microtiter wells. We compared the results of this assay with those of an immunoradiometric assay (IRMA) performed with the same **antibodies** working ranges (CV less than 10%) were 25 to 1000 ng/L and 22 to 1000 ng/L for the IFMA and IRMA, respectively, and both assays had comparable detection limits (IFMA 4.0 +/- 1 ng/L, IRMA 3.5 +/- 0.8 ng/L). Results by both assays for 130 patients' samples containing corticotropin within the range 3-100 ng/L and greater than ng/L correlated well (r = 0.88 and 0.92, respectively), and samples with corticotropin in the range 80-624 ng/L gave results that paralleled those for the standard curve. Corticotropin concentrations in apparently healthy subjects were consistent with those reported previously. The IFMA is a simple, precise, and robust assay that can be completed within one day. Its nonisotopic label is stable for at least 50 weeks.

L8 ANSWER 61 OF 68 MEDLINE on STN DUPLICATE 38

87103690 Document Number: 87103690. PubMed ID: 3026691. Clinical evaluation of a two-site immunoradiometric assay for adrenocorticotrophin in unextracted human plasma using monoclonal **antibodies**. White A; Smith H; Hoadley M; Dobson S H; Ratcliffe J G. CLINICAL ENDOCRINOLOGY, (1987 Jan) 26 (1) 41-51. Journal code: 0346653. ISSN: 0300-0664. Pub. country: ENGLAND: United Kingdom. Language: English.

AB We have developed a sensitive two-site immunoradiometric assay (IRMA) for intact ACTH and its precursors, pro-opiomelanocortin and 22 kDa peptide in unextracted human plasma. The assay uses two monoclonal **antibodies**. **Antibody** 1A12, specific for ACTH 10-18, is radiolabelled and **antibody 2A3** specific for the C-terminal region (ACTH 24-39), is coupled to Sephacryl S300 for the solid-phase. Samples are incubated for 18 h with labelled **antibody** followed by 2 h with solid-phase **antibody**. Separation employs the sucrose layering technique. Using human pituitary ACTH 1-39 (code 74/555) in diluent containing 10% horse serum to standardize the assay, the sensitivity (upper 99% confidence limit of zero standard) is 3.5 +/- 0.8 ng/l (n - 7). The mean coefficient of variation is 5.9% within-assay and 6.7% between-assay and is less than 10% between 22 and greater than 5000 ng/l. Mean recovery of ACTH 1-39 added to dexamethasone-suppressed human plasma is 109% and endogenous ACTH behaves indistinguishably from standard ACTH on dilution. In normal subjects, mean plasma ACTH levels are 30 ng/l at 0730 h, and 15 ng/l at 1630 h at rest. ACTH concentrations are between 60 and 330 ng/l, 8-10.5 h after metyrapone (2 g orally at 2300 h), between 140 and 320 ng/l, 30-60 min after insulin-induced hypoglycaemia, and less than 4 ng/l, 8 h after dexamethasone (1.5 mg orally at 2300 h). In a range of pathological conditions ACTH concentrations accurately reflect the disorders of the pituitary-adrenal axis. Endogenous ACTH immunoactivity is stable in vitro at 22 degrees C for at least 1 h in whole blood and at least 4 h in plasma. It is concluded that this two-site IRMA for ACTH in unextracted plasma offers a reliable assay for clinical purposes.

L8 ANSWER 62 OF 68 MEDLINE on STN DUPLICATE 39

87075615 Document Number: 87075615. PubMed ID: 3098233. Monoclonal **antibodies** to the guanine-nucleotide binding proteins of adenylate cyclase. Lingham R B; Brown P J; Holcombe V; Schreiber C L. BIOCHEMICAL JOURNAL, (1986 May 15) 236 (1) 267-71. Journal code: 2984726R. ISSN: 0264-6021. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Monoclonal **antibodies** (Mabs) to the stimulatory (Ns) and inhibitory (Ni) guanine nucleotide regulatory proteins associated with adenylate cyclase have been developed. Two Mabs (**2A3** and 5G12), which are of the IgG2b subclass, recognize the beta-subunits (beta) of Ns, Ni and transducin. Iodinated beta can be immunoprecipitated by either Mab coupled to Affi-Gel 10 and this can be decreased by prior incubation of the Mabs with excess unlabelled beta. The Mabs stabilize the activated state of Ns while decreasing the rate of deactivation of activated Ns in the presence of beta.

L8 ANSWER 63 OF 68 MEDLINE on STN DUPLICATE 40

86169733 Document Number: 86169733. PubMed ID: 2420898. Selection and optimisation of monoclonal **antibodies** for a two-site immunoradiometric assay for ACTH. Dobson S H; Gray C; Smith H; Baker T; Ratcliffe J G; White A. JOURNAL OF IMMUNOLOGICAL METHODS, (1986 Apr 3) 88 (1) 83-90. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB Four monoclonal **antibodies** with predominant specificities towards different sequences within the ACTH molecule were investigated in a 2-site immunoradiometric assay (IRMA) for human ACTH. **Antibody** 3H9 recognises the extreme N-terminal sequence, **antibodies** 1A12 and 1D1 are specific for the mid N-terminal sequence but differ in that the former cross-reacts with alpha MSH whereas the latter does not, and **antibody 2A3** recognises the C-terminal sequence. Combinations of iodinated **antibodies** with **antibodies** covalently linked to Sephacryl S300 were tested for their compatibility and potential for a sensitive assay. Two **antibody** combinations (1D1 plus 3H9 or 1A12) gave no dose-response curve indicating severe steric inhibition, whereas other combinations yielded assays with widely different detection limits (2-2400 ng ACTH/l). The combination of labelled 1D1 and solid-phase **2A3** gave the most sensitive assay and when optimised for **antibody** concentrations and incubation times the working range was 10-5 X 10(4) ng/l (CV less than 20%). The optimised sequential 2-step IRMA involves incubation of standard or test sample with labelled 1D1 for 18 h at 4 degrees C followed by incubation with solid-phase **2A3** for 2 h at room temperature, after which the labelled complex is separated by the sucrose layering technique. The detection limit of this IRMA was several 100-fold lower than by RIA using the same **antibodies**. The IRMA detected large molecular weight precursors containing the full ACTH sequence (22 000, 31 000 and 34 000) but not ACTH fragments (1-18, 1-24, 18-39). It is concluded that selected monoclonal **antibodies** provide a sensitive and rapid 2-site IRMA for intact ACTH and its precursors.

L8 ANSWER 64 OF 68 MEDLINE on STN DUPLICATE 41

86094284 Document Number: 86094284. PubMed ID: 3936041. Induction and upregulation by interleukin 2 of high-affinity interleukin 2 receptors on thymocytes and T cells. Reem G H; Yeh N H; Urdal D L; Kilian P L; Farrar J J. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1985 Dec) 82 (24) 8663-6. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB We show that purified recombinant interleukin 2 (rIL-2) alone induces the expression of high- and low-affinity interleukin 2 (IL-2) receptors in vitro on human T cells and thymocytes that have not been activated previously by lectins or other inducing agents. IL-2 receptors are expressed after 24 hr, as determined by the binding of 125I-labeled monoclonal anti-IL-2 receptor **antibody 2A3**, which binds equally to high- and low-affinity receptors. High-affinity receptors were distinguished from low-affinity receptors by the binding of 125I-labeled IL-2 to T cells and by the proliferative response of thymocytes to IL-2, in concentrations that selectively interact with the high-affinity class of IL-2 receptors. The IL-2-induced proliferation of thymocytes in vitro induced by IL-2 alone is dependent upon the concentration of IL-2 and is inhibited by monoclonal anti-Tac **antibody**, indicating that the proliferative response is mediated by the binding of IL-2 to the receptors. In addition, we demonstrate that IL-2 augments the number of high-affinity receptors on concanavalin A-activated thymocytes. These results document that IL-2 acts as a hormone that induces the activation of thymocytes and T cells, as evidenced by the de novo induction of biologically active, high-affinity IL-2 receptors. IL-2 also upregulates the expression of high-affinity IL-2 receptors on activated thymocytes. These observations illustrate the biologic importance of the regulatory role of IL-2 in the immune response.

L8 ANSWER 65 OF 68 MEDLINE on STN DUPLICATE 42
85262918 Document Number: 85262918. PubMed ID: 3926896. Induction of **antibody** responses to influenza virus in human lymphocyte cultures. I. Role of interleukin 2. Tan P L; Booth R J; Prestidge R L; Watson J D; Dower S K; Gillis S. JOURNAL OF IMMUNOLOGY, (1985 Sep) 135 (3) 2128-33. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The in vitro T cell-dependent **antibody** response of human lymphocytes to influenza virus X31 was used to study the role of T cell-derived lymphokines in antigen-specific responses. Supernatant from cultures of phytohaemagglutinin-stimulated, pooled human tonsil cells (PHA-MLR) was capable of replacing T cells and inducing T-depleted tonsil cells to secrete influenza-specific **antibody**. The T cell-replacing activity of PHA-MLR supernatant co-purified with interleukin 2 (IL 2) on Ultrogel AcA54 gel filtration and reversed phase-high performance liquid chromatography. PHA-MLR supernatant and IL 2 also enhanced B cell proliferation induced by anti-mu or Staphylococcal aureus strain Cowan I (SAC). A murine monoclonal **antibody** directed against the human IL 2 receptor (Mab **2A3**) was used to completely block the enhancement of influenza-specific **antibody** production mediated by PHA-MLR supernatant, purified IL 2, and recombinant human IL 2. Mab **2A3** did not affect the T-independent B cell proliferation induced by anti-mu or SAC, but abrogated the enhancing effect of the PHA-MLR supernatant and IL 2 in this culture system. Immunofluorescence studies failed to demonstrate binding of Mab **2A3** to B cells activated by the X31 influenza virus and IL 2, or by SAC. By using Mab **2A3** to mask out IL 2 effects in the influenza-specific culture system, no other B cell differentiating activities were revealed in supernatants from lymphocytic cultures stimulated with a variety of mitogens. Thus, our results indicate that the production of influenza-specific **antibodies** by T-depleted human lymphocyte cultures is absolutely dependent on the presence of both antigen and IL 2.

L8 ANSWER 66 OF 68 MEDLINE on STN DUPLICATE 43
86014023 Document Number: 86014023. PubMed ID: 3930953. Quantitative measurement of human interleukin 2 receptor levels with intact and detergent-solubilized human T-cells. Dower S K; Hefeneider S H; Alpert A R; Urdal D L. MOLECULAR IMMUNOLOGY, (1985 Aug) 22 (8) 937-47. Journal code: 7905289. ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.

AB **2A3** monoclonal **antibody** (gamma 1, kappa) is a novel high-affinity reagent for detecting the human interleukin 2 (IL-2) receptor. The **antibody** inhibits IL-2 binding to its receptor and is an antagonist of IL-2 action. Detailed analysis of the mechanism of binding of the IgG, (Fab')2 and Fab' of **2A3 antibody** shows that the bivalent species cross-link on the cell surface when bound. Measurements of IL-2 receptor expression on digitonin-permeabilized cells suggest that the intracellular pool of receptors is small. The **antibody** will bind to IL-2 receptors on glutaraldehyde-fixed cells in the presence of Triton X-100. This property is used in designing an assay for quantitative measurements of IL-2 receptor concn in solution. This assay can be used to monitor receptor protein during purification to homogeneity.

L8 ANSWER 67 OF 68 MEDLINE on STN DUPLICATE 44
85209286 Document Number: 85209286. PubMed ID: 2582058. Characterisation of monoclonal **antibodies** to adrenocorticotrophin. White A; Gray C; Ratcliffe J G. JOURNAL OF IMMUNOLOGICAL METHODS, (1985 May 23) 79 (2) 185-94. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB We have produced 8 monoclonal **antibodies** to adrenocorticotrophin (ACTH) derived from immunisation with ACTH (1-24) conjugated to bovine

serum albumin or ACTH (1-39) linked to chicken immunoglobulin by a novel method. **Antibody** specificity was assessed by studying the binding of purified human ACTH, synthetic ACTH (1-24), fragments of ACTH and peptides from the ACTH precursor molecule which have sequence homology. A wide range of specificities was demonstrated. Thus **antibody** 3H9 recognises the extreme N-terminal sequence (ACTH 4-10), **antibody** 1A12 is specific for residues 10-18 including alpha MSH, **antibody** 1D1 is specific for the mid N-terminal sequence but not alpha MSH, and **antibody 2A3** is specific for the C-terminal portion (ACTH 18-39). These monoclonal **antibodies** can be easily purified and labelled and their defined specificities make it possible to select **antibody** combinations which provide the basis for 2-site immunometric assays for ACTH.

L8 ANSWER 68 OF 68 CAPLUS COPYRIGHT 2003 ACS on STN
1985:143996 Document No. 102:143996 Molecular basis of an isogeneic anti-idiotypic response. Sablitzky, Fred; Rajewsky, Klaus (Inst. Genet., Univ. Koeln, Cologne, Fed. Rep. Ger.). EMBO Journal, 3(12), 3005-12 (English) 1984. CODEN: EMJODG. ISSN: 0261-4189.
AB The nucleotide sequences of the variable region genes expressed in the heavy and light chains of 6 isogenic anti-idiotope **antibodies** recognizing idiotopes on 2 closely related **antibodies** with specificity for the hapten group (4-hydroxy-3-nitrophenyl)acetyl [6322-56-1] were detd. In 2 independently derived anti-idiotope cell lines, the same or strongly homologous V.kappa., VH, and D region genes had originally been rearranged. The 2 lines express long and partly homologous N sequences (presumably not of germ-line origin) at the border of D, resulting in complementarity-detg. region 3 (CDR3) of unusual length. An unusually long CDR3, partly encoded by N sequences, is also present in the heavy chain of a 3rd anti-idiotope **antibody**. The VH regions of the 3 remaining anti-idiotope **antibodies** originate from a single VH gene which belongs to the same VH group as the VH genes expressed in the other anti-idiotopes. Two of these **antibodies**, expressing similar V, D, and J elements, had been isolated from the same mouse and appear to have diverged from the same B cell precursor by .gtoreq.2 rounds of somatic mutation. Somatic point mutations have occurred in most, if not all anti-idiotope V region sequences. In 2 instances, somatic mutations in J increase the structural homol. between anti-idiotopes. The anti-idiotypic response in this system is, thus, genetically restricted and may depend upon the selection of non-germ line sequences, suggesting an explanation for the low frequency at which anti-idiotope **antibodies** are expressed in this system. .

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=> s l1 adn "2A8"
MISSING OPERATOR L1 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l1 and "2A8"
L9          66 L1 AND "2A8"

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10         28 DUP REMOVE L9 (38 DUPLICATES REMOVED)

=> s l10 and "EG-VEGF"
L11          1 L10 AND "EG-VEGF"

=> d l11 cbib abs

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
2002:964996 Document No. 138:33697 Endocrine gland-derived vascular
    endothelial growth factor nucleic acids and polypeptides and their
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biological activities and use in drug screening and therapies. Ferrara, Napoleone; Watanabe, Colin; Wood, William I.; Shek, Theresa (USA). U.S. Pat. Appl. Publ. US 2002192634 A1 20021219, 105 pp., Cont.-in-part of U.S. Ser. No. 886,242. (English). CODEN: USXXCO. APPLICATION: US 2001-27603 20011219. PRIORITY: US 1998-PV96146 19980811; WO 1999-US12252 19990602; US 1999-PV145698 19990726; US 1999-380137 19990825; WO 2000-US219 20000105; WO 2000-US4914 20000224; WO 2000-US8439 20000330; US 2000-PV213637 20000623; US 2000-PV230978 20000907; US 2000-709238 20001108; WO 2000-US32678 20001201; US 2001-886242 20010620.

AB The present invention is based on the identification and characterization of a novel, tissue-restricted, growth and differentiation factor that acts selectively on one endothelial cell type. This factor, referred to as endocrine gland-derived vascular endothelial growth factor (**EG-VEGF**), induces proliferation, migration, and fenestrations in capillary endothelial cells derived from endocrine glands, but has no effect on a variety of other endothelial and non-endothelial cell types tested. **EG-VEGF** also induces phosphorylation of kinases involved in cell proliferation or survival, including ERK1, ERK2, Akt, and eNOS. **EG-VEGF** nucleic acids and polypeptides can be used in a no. of assays and in diagnosis and treatment of conditions assocd. with hormone-producing tissue. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, **antibodies** which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Also provided herein are methods of screening for modulators of **EG-VEGF**. Furthermore, methods and related methods of treatment are described herein which pertain to regulating cellular proliferation and chemotaxis.

=> d l10 1-28 cbib abs

L10 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN

2003:320041 Document No. 138:335903 Identification of genes expressed in skeletal muscle associated with abnormal glucose tolerance for diagnosis of type 2 diabetes mellitus using microarrays. Lindgren, Cecilia M.; Hirschhorn, Joel N.; Tamayo, Pablo; Daly, Mark J.; Lander, Eric S.; Altshuler, David M. (Whitehead Institute for Biomedical Research, USA; The General Hospital Corporation; University of Lund). PCT Int. Appl. WO 2003033676 A2 20030424, 54 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US33524 20021017. PRIORITY: US 2001-PV330147 20011017.

AB The present invention features method for identifying an individual having impaired glucose tolerance, impaired glucose homeostasis and/or type 2 diabetes mellitus according to gene expression profiles of informative genes. The present invention also features methods of identifying a compd. that modulates impaired glucose tolerance, impaired glucose homeostasis and/or type 2 diabetes mellitus, as well oligonucleotide microarrays having immobilized thereon one or more probes for one or more informative genes.

L10 ANSWER 2 OF 28 MEDLINE on STN DUPLICATE 1

2003118634 Document Number: 22519426. PubMed ID: 12631475. Adherence of Mycoplasma bovis to bovine bronchial epithelial cells. Thomas A; Sachse K; Farnir F; Dizier I; Mainil J; Linden A. (Department of Infectious and Parasitic Diseases, Faculty of Veterinary Medicine, University of Liege,

B43A, Sart Tilman, 4000, Liege, Belgium.. athomas@ulg.ac.be) . MICROBIAL PATHOGENESIS, (2003 Mar) 34 (3) 141-8. Journal code: 8606191. ISSN: 0882-4010. Pub. country: England: United Kingdom. Language: English.

AB Mycoplasma bovis is responsible for considerable economic losses in cattle due to pneumonia, arthritis and mastitis. As the agent was shown to be capable of adhering to neutrophils and embryonic bovine lung (EBL) cells and invading the respiratory epithelium it is highly desirable to improve our understanding of cytadherence processes. Although several surface proteins likely to be directly involved in this initial stage of interaction between pathogen and host cells have been identified, these findings mainly referred to type strain PG45 adhering to the continuous EBL cell line.The present study provides new and complementary data about cytadherence of M. bovis based on adherence of various radiolabeled strains to a primary culture of bovine bronchial epithelial (BBE) cells using a standardized adherence assay. M. bovis was shown to adhere specifically to the primary culture of BBE cells. Inhibition of adherence was observed upon addition of monoclonal **antibodies** (MAbs), trypsin treatment of mycoplasmas, and competition with non-radiolabeled mycoplasma cells. Interestingly, three MAbs against proteins involved in adherence to EBL cells failed to inhibit significantly the adherence to BBE cells. On the other hand, significant reduction of adherence rates by MAbs **2A8** and 9F1 directed against epitopes of variable surface lipoproteins VspC and VspF, respectively, demonstrated the involvement of these proteins in adherence of M. bovis to primary culture of BBE cells.

L10 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN

2002:637933 Document No. 137:154209 Use of troponin I as a species marker protein for meat speciation in both raw and heat-processed products. Hsieh, Yun-Hwa Peggy; Chen, Fur-Chi (Auburn University, USA). PCT Int. Appl. WO 2002065126 A2 20020822, 37 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US4671 20020215. PRIORITY: US 2001-PV269055 20010215; US 2001-PV286045 20010423.

AB Monoclonal **antibodies** to troponin I are provided which bind to heat-treated proteins of meats. The **antibodies** are useful in detecting the presence of an exogenous meat in a cooked or raw meat sample. Furthermore, the **antibodies** can be used to det. the end point temp. of a meat sample.

L10 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN

2002:964996 Document No. 138:33697 Endocrine gland-derived vascular endothelial growth factor nucleic acids and polypeptides and their biological activities and use in drug screening and therapies. Ferrara, Napoleone; Watanabe, Colin; Wood, William I.; Shek, Theresa (USA). U.S. Pat. Appl. Publ. US 2002192634 A1 20021219, 105 pp., Cont.-in-part of U.S. Ser. No. 886,242. (English). CODEN: USXXCO. APPLICATION: US 2001-27603 20011219. PRIORITY: US 1998-PV96146 19980811; WO 1999-US12252 19990602; US 1999-PV145698 19990726; US 1999-380137 19990825; WO 2000-US219 20000105; WO 2000-US4914 20000224; WO 2000-US8439 20000330; US 2000-PV213637 20000623; US 2000-PV230978 20000907; US 2000-709238 20001108; WO 2000-US32678 20001201; US 2001-886242 20010620.

AB The present invention is based on the identification and characterization of a novel, tissue-restricted, growth and differentiation factor that acts selectively on one endothelial cell type. This factor, referred to as endocrine gland-derived vascular endothelial growth factor (EG-VEGF), induces proliferation, migration, and fenestrations in capillary endothelial cells derived from endocrine glands, but has no effect on a variety of other endothelial and non-endothelial cell types tested.

EG-VEGF also induces phosphorylation of kinases involved in cell proliferation or survival, including ERK1, ERK2, Akt, and eNOS. EG-VEGF nucleic acids and polypeptides can be used in a no. of assays and in diagnosis and treatment of conditions assocd. with hormone-producing tissue. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, **antibodies** which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Also provided herein are methods of screening for modulators of EG-VEGF. Furthermore, methods and related methods of treatment are described herein which pertain to regulating cellular proliferation and chemotaxis.

L10 ANSWER 5 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
2003:95904 Document No.: PREV200300095904. Anti-Concholepas concholepas hemocyanin (anti-CCH **2A8**). Becker, Maria Ines [Reprint Author]. BIOSONDA S.A., Eduardo Castillo Velasco 2902, Santiago, Chile. mib@biosonda.cl. Hybridoma and Hybridomics, (December 2002) Vol. 21, No. 6, pp. 503. print.
ISSN: 1536-8599 (ISSN print). Language: English.

L10 ANSWER 6 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 2
2002:602072 Document No.: PREV200200602072. Monoclonal **antibodies** against troponin I for the detection of rendered muscle tissues in animal feedstuffs. Chen, Fur-Chi; Hsieh, Y.-H. Peggy [Reprint author]; Bridgman, Roger C.. Department of Nutrition and Food Science, Auburn University, Auburn, AL, 36849, USA. hsiehyp@auburn.edu. Meat Science, (December, 2002) Vol. 62, No. 4, pp. 405-412. print.
CODEN: MESCDN. ISSN: 0309-1740. Language: English.
AB Regulatory controls to prevent the spread of BSE have prohibited the use of certain animal proteins in feed in several countries. Accurate analytical methods for detecting prohibited material in feedstuffs are needed to ensure compliance with the new regulations. Six IgG class monoclonal **antibodies** (MAbs) against troponin I (TnI), a thermostable marker protein, have been developed for the detection and differentiation of rendered muscle tissue in animal feed. MAbs 1F9, 2G3 and 7F7 reacted to TnI of all species, including mammalian, poultry and fish, while MAbs 7A12 and 8A12 recognized only mammalian TnI (porcine, bovine, ovine, equine, and deer). MAb **2A8** was able to differentiate TnI of ruminant origin (bovine, ovine and deer) from other species. Three indirect enzyme-linked immunosorbent assays (ELISAs) employing these MAbs were developed for the determination of animal muscle, mammalian muscle or ruminant muscle in animal feeds.

L10 ANSWER 7 OF 28 MEDLINE on STN DUPLICATE 3
2002709029 Document Number: 22358794. PubMed ID: 12470479. Monoclonal **antibodies** to molluskan hemocyanin from Concholepas concholepas demonstrate common and specific epitopes among subunits. Oliva Harold; Moltedo Bruno; De Ioannes Pablo; Faunes Fernando; De Ioannes Alfredo E; Becker Maria Ines. (Department of Research and Development, BIOSONDA Corp, Eduardo Castillo Velasco 2902, Santiago, Chile.) Hybrid Hybridomics, (2002 Oct) 21 (5) 365-74. Journal code: 101131136. ISSN: 1536-8599. Pub. country: United States. Language: English.
AB We studied the reactivity of mouse monoclonal **antibodies** (MAbs) against the hemocyanin from the Chilean marine gastropod Concholepas concholepas (CCH). This protein has been successfully used as a carrier to produce **antibodies** to haptens and peptides. All MAbs (13) belonging to IgG subclass exhibit dissociation constants (K(d)) from 1 x 10(-7) M to 1 x 10(-9) M. MAbs were characterized by enzyme-linked immunosorbant assay (ELISA) using CCH treated with different procedures, including dissociation into CCH-A and CCH-B subunits, Western blot, enzymatic digestion, chemical deglycosylation, and thermal denaturation.

MAbs were classified into three categories, according to subunit specificity by ELISA. The epitope distribution shows that CCH subunits display common epitopes (group I, 5 MAbs, 1H5, **2A8**, 3A5, 3B3, and 3E3), as well as specific epitopes for CCH-A subunits (group II, 3 MAbs, 1B8, 4D8, and 8E5) and for CCH-B subunits (group III, 5 MAbs, 1A4, 1E4, 2H10, 3B7, and 7B4). The results can be summarized as follows: (1). six **antibodies** react with thermal denatured CCH, suggesting that they recognize linear epitopes, whereas seven recognize conformational epitopes; (2). oxidation of carbohydrate moieties does not affect the binding of the MAbs; (3). enzymatic digestion of CCH decreases the reactivity of all **antibodies** irrespective of the protease used (elastase or trypsin); (4). bringing together the above data, in addition to epitopic complementarity analysis, we identified 12 different epitopes on the CCH molecule recognized by these MAbs. The anti-CCH MAbs presented here can be useful tools to understand the subunit organization of the CCH and its complex structure, which can explain its immunogenic and immunostimulating properties in mammals.

L10 ANSWER 8 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
2002:906170 The Genuine Article (R) Number: 612JV. Monoclonal **antibodies** to molluskan hemocyanin from Concholepas concholepas demonstrate common and specific epitopes among subunits. Oliva H; Moltedo B; De Ioannes P; Faunes F; De Ioannes A E; Becker M I (Reprint). BIOSANDA Corp, Dept Res & Dev, Immunol Lab, Santiago 2902, Chile (Reprint). HYBRIDOMA AND HYBRIDOMICS (OCT 2002) Vol. 21, No. 5, pp. 365-374. Publisher: MARY ANN LIEBERT INC PUBL. 2 MADISON AVENUE, LARCHMONT, NY 10538 USA. ISSN: 0272-457X. Pub. country: Chile. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We studied the reactivity of mouse monoclonal **antibodies** (MAbs) against the hemocyanin from the Chilean marine gastropod Concholepas concholepas (CCH). This protein has been successfully used as a carrier to produce **antibodies** to haptens and peptides. All MAbs (13) belonging to IgG subclass exhibit dissociation constants (K-d) from 1 x 10(-7) M to 1 x 10(-9) M. MAbs were characterized by enzyme-linked immunosorbant assay (ELISA) using CCH treated with different procedures, including dissociation into CCH-A and CCH-B subunits, Western blot, enzymatic digestion, chemical deglycosylation, and thermal denaturation. MAbs were classified into three categories, according to subunit specificity by ELISA. The epitope distribution shows that CCH subunits display common epitopes (group I, 5 MAbs, 1H5, **2A8**, 3A5, 3B3, and 3E3), as well as specific epitopes for CCH-A subunits (group II, 3 MAbs, 1B8, 4D8, and 8E5) and for CCH-B subunits (group III, 5 MAbs, 1A4, 1E4, 2H10, 3B7, and 7B4). The results can be summarized as follows: (1) six **antibodies** react with thermal denatured CCH, suggesting that they recognize linear epitopes, whereas seven recognize conformational epitopes; (2) oxidation of carbohydrate moieties does not affect the binding of the MAbs; (3) enzymatic digestion of CCH decreases the reactivity of all **antibodies** irrespective of the protease used (elastase or trypsin); (4) bringing together the above data, in addition to epitopic complementarity analysis, we identified 12 different epitopes on the CCH molecule recognized by these MAbs. The anti-CCH MAbs presented here can be useful tools to understand the subunit organization of the CCH and its complex structure, which can explain its immunogenic and immunostimulating properties in mammals.

L10 ANSWER 9 OF 28 MEDLINE on STN DUPLICATE 4
1999333487 Document Number: 99333487. PubMed ID: 10403757. Acanthamoeba castellanii: characterization of an adhesin molecule. Kennett M J; Hook R R Jr; Franklin C L; Riley L K. (Department of Veterinary Pathobiology, College of Veterinary Medicine, University of Missouri-Columbia, Columbia, Missouri, 65211, USA.) EXPERIMENTAL PARASITOLOGY, (1999 Jul) 92 (3) 161-9. Journal code: 0370713. ISSN: 0014-4894. Pub. country: United States. Language: English.

AB Acanthamoeba castellanii is a free-living protozoan that causes keratitis

in humans and has been associated with pneumonia and granulomatous amebic encephalitis in dogs, sheep, and other species. Adherence of the Acanthamoeba to epithelial cells is critical to the pathogenesis of this disease. In this study, several mouse monoclonal **antibodies** (MAb) generated to whole Acanthamoeba trophozoites identified surface membrane epitopes by ELISA and IFA. Nine **antibodies** inhibited adherence of [(35)S]-methionine-labeled Acanthamoeba trophozoites to hamster corneal epithelial cells by 27-90%. Sodium periodate treatment, but not proteinase K digestion, of whole Acanthamoeba destroyed epitopes recognized by adherence-inhibiting **antibodies** such as MAb 7H6, suggesting that the adherence epitopes are carbohydrates. Other **antibodies**, MAb **2A8** for example, recognized surface membrane peptide epitopes that were proteinase K sensitive and sodium periodate resistant. Purified MAb **2A8** was used in an antigen-capture ELISA with peroxidase-labeled MAb 7H6 and demonstrated that the carbohydrate adhesion molecule was linked to the peptide recognized by MAb **2A8**. Both MAbs 7H6 and **2A8** recognized a >207-kDa band on a Western blot of eluant from a MAb **2A8** immunoaffinity column, confirming that MAb 7H6 and MAb **2A8** recognize different epitopes on the same adherence molecule. MAbs 7H6 and **2A8** also identified the adhesion molecule in soluble Acanthamoeba membrane preparations and MAb **2A8** immunoaffinity column eluant by ELISA and Western blot. Neither of these **antibodies** were inhibited from binding to whole trophozoites nor membrane extracts by mannose or mannan in competitive binding assays. When our Acanthamoeba membrane preparations were electrophoresed and immunoblotted with alpha-d-mannosylated-biotin albumin, no bands were recognized in the >207 kDa range by our adherence-associated **antibodies**. These results suggest that the Acanthamoeba adhesin is not identical to the mannose binding protein of Acanthamoeba but rather is a distinct surface membrane glycoprotein.

L10 ANSWER 10 OF 28 MEDLINE on STN DUPLICATE 5

1999049845 Document Number: 99049845. PubMed ID: 9834099. Cloning and characterization of the guinea pig eosinophil eotaxin receptor, C-C chemokine receptor-3: blockade using a monoclonal **antibody** in vivo. Sabroe I; Conroy D M; Gerard N P; Li Y; Collins P D; Post T W; Jose P J; Williams T J; Gerard C J; Ponath P D. (Biomedical Sciences Division, Imperial College School of Medicine, London, United Kingdom.) JOURNAL OF IMMUNOLOGY, (1998 Dec 1) 161 (11) 6139-47. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Certain C-C chemokines, signaling via the eotaxin receptor C-C chemokine receptor-3 (CCR3), are thought to be central mediators of eosinophil accumulation in allergic inflammation. To investigate the role of CCR3 in vivo, we cloned the guinea pig eotaxin receptor (guinea pig CCR3) from a genomic DNA library. We isolated a single-exon open reading frame coding for a 358-amino acid chemokine receptor protein with 67 and 69% homology to human and murine CCR3, respectively. When expressed in stable transfectants, this receptor bound 125I-labeled guinea pig eotaxin, 125I-labeled human monocyte chemotactic protein-3, and 125I-labeled human RANTES. In chemotaxis assays, guinea pig CCR3 transfectants responded only to guinea pig eotaxin, with a maximal effect at 100 nM. mAbs were raised that bound selectively to both guinea pig CCR3 transfectants and guinea pig eosinophils. One of these mAbs, **2A8**, blocked both ligand binding to transfectants and their chemotaxis in response to eotaxin. The Ab also inhibited chemotaxis and the elevation of cytosolic calcium in guinea pig eosinophils in response to eotaxin. F(ab')2 fragments of **2A8** were prepared that retained the ability to inhibit eosinophil calcium responses to eotaxin. Pretreatment of (111)In-labeled eosinophils in vitro with F(ab')2 **2A8** selectively inhibited their accumulation in response to eotaxin in vivo. These data demonstrate that functional blockade of eosinophil chemokine receptors can be achieved in vivo and provide further support for the

development of novel anti-inflammatory drugs targeting eosinophil recruitment through chemokine receptor antagonism.

L10 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
1998:548899 Document No. 129:288897 Intrasplenic injection of antigens for efficient preparation of monoclonal **antibodies**. Ma, Yingze; Li, Xiaomei; Lu, Yanjuan; Yang, Hanyi; Hu, Xiuying (School Basic Med. Sci., Norman Bethune Univ. Med. Sci., Changchun, 130021, Peop. Rep. China). Zhongguo Shouyi Xuebao, 18(3), 260-261 (Chinese) 1998. CODEN: ZSXUF5. ISSN: 1005-4545. Publisher: Zhongguo Shouyi Xuebao Bianjibu.
AB A speedy and efficient method for the prepn. of monoclonal **antibody** to human chorionic gonadotropin (hCG) by intrasplenic injection of hCG into BALB/c mice is disclosed. On 5th day after immunization, the spleen cells from the mice having the serum titer .gtoreq.1:12,800 were fused with myeloma cells NS-1. Ascitic culture of 2 monoclonal lines, **2A8** and 4E6, in BALB/c mice gave 10-6 and 10-5 titers, resp.

L10 ANSWER 12 OF 28 MEDLINE on STN DUPLICATE 6
97329599 Document Number: 97329599. PubMed ID: 9186073. Interleukin-8 expression in patients after renal transplantation. Budde K; Waiser J; Ceska M; Katalinic A; Kurzdorfer M; Neumayer H H. (Department of Internal Medicine-Nephrology, Charite, Humboldt University, Berlin, Germany.) AMERICAN JOURNAL OF KIDNEY DISEASES, (1997 Jun) 29 (6) 871-80. Journal code: 8110075. ISSN: 0272-6386. Pub. country: United States. Language: English.
AB Cellular invasion and cytokine release are important steps in the initiation of rejection. We studied the release of interleukin-8 (IL-8), a potent proinflammatory and chemotactic cytokine, and its prognostic significance in predicting rejection after renal transplantation. Serum and urine samples were analyzed with an IL-8-specific sandwich enzyme-linked immunosorbent assay. Biopsy tissue specimens (n = 20) were snap-frozen and examined with immunohistochemistry using two monoclonal **antibodies** against human IL-8 (4G9 and **2A8**). Serum IL-8 measurements were of no value in predicting rejection due to low sensitivity (24%). In 45 biopsy-proven acute rejections (< 2 months after transplantation), urinary IL-8 concentrations were elevated in 62% (298 +/- 54 pg/mL; P < 0.01), preceding clinical diagnosis of rejection. After treatment, the IL-8 concentration in urine decreased back to normal (33 +/- 4 pg/mL; P < 0.01). The highest urinary IL-8 concentrations were seen in patients with biopsy-proven rejection in combination with acute tubular necrosis (610 +/- 150 pg/mL). This finding was independent of renal function and urinary volume. Only three of 15 rejection episodes in patients more than 2 months after transplantation showed an elevated IL-8 concentration in urine (94 +/- 60 pg/mL). In 10 of 23 patients with infection, a significant increase of IL-8 in urine was observed as well (157 +/- 67 pg/mL; P < 0.05). IL-8-positive staining was found within interstitial mononuclear cells of all biopsy specimens showing rejection. Additionally, the **antibody** 4G9 stained arteriolar smooth muscle and tubular cells. Interestingly, a few IL-8-positive cells were present in two donor kidneys before transplantation was performed; control tissue was negative. Further investigations are necessary to determine the clinical value of urinary IL-8 determinations in the diagnosis of rejection and to evaluate the role of IL-8 in the pathogenesis of acute allograft rejection.

L10 ANSWER 13 OF 28 MEDLINE on STN DUPLICATE 7
1998047217 Document Number: 98047217. PubMed ID: 9388024. Pharmacokinetics, tolerability, and preliminary efficacy of human anti-Pseudomonas aeruginosa monoclonal **antibodies** in pneumonia and burn infection patients. Harrison F J; Rohm D; Kohzuki T; Noguchi H. (Harrison Clinical Research GmbH, Munchen, Germany.) HYBRIDOMA, (1997 Oct) 16 (5) 413-20. Journal code: 8202424. ISSN: 0272-457X. Pub. country: United States. Language: English.

AB Human monoclonal **antibody** (hMAb) cocktail SM-17220 (also known as BT-570), a heterofunctional **antibody** mixture of 3 human IgM MAbs (HI-223, MH-4H7, and IN-**2A8**; ratio of 1:10:10) directed against Pseudomonas aeruginosa, were administered to patients with pneumonia or burn wounds (or both) to assess the pharmacokinetics, safety, antigenicity, and preliminary efficacy. Twenty mg of SM-17220 was IV infused over 60 min once daily on 3 consecutive days. Twenty patients (8 pneumonia, 4 burns, and 8 both) completed the study. SM-17220 was safe and well tolerated, and no subjects developed **antibodies** to SM-17220 and mouse J-chain during the follow-up of 8 weeks. Each MAb of SM-17220 had a half-life ranging from 49 to 91 h, similar to native human IgM. Both MH-4H7 and IN-**2A8** administration resulted in a high serum level for about 4 days over an effective concentration, whereas HI-223 showed a lower serum level than expected. Some indications of a potential efficacy were observed and are discussed here.

L10 ANSWER 14 OF 28 EMBASE
on STN
96324724 EMBASE Document No.: 1996324724. Hamster liver cytochrome P450 (CYP2A8) as a 4-hydroxylase for 2,5,2',5'-tetrachlorobiphenyl. Koga N.; Kikuichi N.; Kanamaru T.; Ariyoshi N.; Oguri K.; Yoshimura H.. Department of Food and Nutrition, Nakamura Gakuen University, 5-7-1 Befu,Johnan-ku, Fukuoka 814-01, Japan. Biochemical and Biophysical Research Communications 225/2 (685-688) 1996.
ISSN: 0006-291X. CODEN: BBRCA. Pub. Country: United States. Language: English. Summary Language: English.
AB Metabolism of 2,5,2',5'-tetrachlorobiphenyl (TCB) was studied using liver microsomes of hamsters and two hamster P450 isoforms, CYP1A2 and **2A8**. CYP2A8 catalyzed selectively 4-hydroxylation of 2,5,2',5-TCB at a rate of 21.7 pmol/min/nmol P450. In contrast, CYP1A2 showed no activity for hydroxylation of 2,5,2',5'-TCB. Immunological study revealed that rabbit antiserum against CYP2A8 almost completely inhibited the microsomal 4-hydroxylation but that against CYP1A2 did not. It was also shown that the induction pattern of CYP2A8 protein by P450 inducer was similar to that of the 4-hydroxylase activity in hamster liver microsomes. These results suggest that CYP2A8 plays a major role in the 4-hydroxylation of 2,5,2',5'-TCB in hamster liver.

L10 ANSWER 15 OF 28 MEDLINE on STN DUPLICATE 8
97136877 Document Number: 97136877. PubMed ID: 8982254. Molecular cloning of a cDNA encoding an antigen which is salt-stably attached to centrosomes. Angiolillo A; Batova I; Joswig G; Werner D. (University of Perugia, Institute of Cellular and Molecular Biology, Italy.) BIOCHIMICA ET BIOPHYSICA ACTA, (1996 Dec 11) 1309 (3) 194-6. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.
AB A monoclonal **antibody** (MAB **2A8**) was used for expression-cloning of a complete cDNA (1133/5) to a mRNA (3 kb) encoding a murine 76 kDa polypeptide. The N-terminal section of the polypeptide is composed of domains capable to form alpha-helical coiled-coils. Its C-terminus is proline-rich and has characteristics of the Src homology region 3 (SH3). Affinity-purified **antibodies** to a recombinant section of the protein show that the antigen is salt-stably associated with the centrosome throughout the cell cycle.

L10 ANSWER 16 OF 28 SCISEARCH on STN
97:5375 The Genuine Article (R) Number: VX952. Molecular cloning of a cDNA encoding an antigen which is salt-stably attached to centrosomes. Angiolillo A; Batova I; Joswig G; Werner D (Reprint). UNIV PERUGIA, INST CELL & MOL BIOL, I-06123 PERUGIA, ITALY (Reprint); UNIV PERUGIA, INST CELL & MOL BIOL, I-06123 PERUGIA, ITALY; BULGARIAN ACAD SCI, INST BIOL & IMMUNOL, BU-1113 SOFIA, BULGARIA; GERMAN CANC RES CTR, DIV CELLULAR BIOCHEM 0225, D-69009 HEIDELBERG, GERMANY. BIOCHIMICA ET BIOPHYSICA ACTA-GENE STRUCTURE AND EXPRESSION (11 DEC 1996) Vol. 1309, No. 3, pp. 194-196. Publisher: ELSEVIER SCIENCE BV. PO BOX 211, 1000 AE AMSTERDAM,

NETHERLANDS. ISSN: 0167-4781. Pub. country: ITALY; BULGARIA; GERMANY. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A monoclonal **antibody** (MAB **2A8**) was used for expression-cloning of a complete cDNA (1133/5) to a mRNA (3 kb) encoding a murine 76 kDa polypeptide. The N-terminal section of the polypeptide is composed of domains capable to form alpha-helical coiled-coils. Its C-terminus is proline-rich and has characteristics of the Src homology region 3 (SH3). Affinity-purified **antibodies** to a recombinant section of the protein show that the antigen is salt-stably associated with the centrosome throughout the cell cycle.

L10 ANSWER 17 OF 28 MEDLINE on STN DUPLICATE 9

95338179 Document Number: 95338179. PubMed ID: 7613516. Redistribution of nuclear envelope associated antigen during the mitotic cycle. Batova I N; Kyurkchiev S D; Russev R; Kehayov I R. (Department of Immunobiology, Institute of Biology and Immunology, Sofia, Bulgaria.) CELL BIOLOGY INTERNATIONAL, (1995 Apr) 19 (4) 279-90. Journal code: 9307129. ISSN: 1065-6995. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Murine hybridomas were generated to DNA/tight binding proteins complex isolated from the residual nuclear structure following a procedure analogous to that yielding "empty" shells of nuclear envelope. A monoclonal **antibody** designated **2A8** was selected because of its differential immunostaining of mitotic cells of a synchronized mouse fibroblast cell culture L-929. The target antigen was rendered insoluble by a sequence of extractions of isolated nuclei of diverse cell types with detergents, urea, DNase I and alkali thus reproducing some solubility properties of proteins constituting an operationally defined residual nuclear matrix. The cognate polypeptide was localized on a subset of proteins of M(r) 58-65 kDa, 70 kDa in isolated fibroblast nuclear matrices. The functional implication of the antigen in mitosis-related disassembly-assembly process of the nuclear matrix/envelope was detected. At prophase the **antibody** decorated the nuclear periphery and nuclear envelope fixed inward filaments. A fibrous network of cytoplasmic localization was stained in metaphase. At anaphase the antigen was dispositioned into peripheral fibrogranular clusters of polar orientation predominantly on one side of the nucleus. Proceeding to telophase a spreading fluorescence was manifested over the entire contour of the nuclear periphery to delineate the reforming nucleus. By immunogold electron microscopy of interphase cells the antigen was identified as evenly distributed in chromatin and interchromatin regions. At initiation of chromosome condensation in mitosis the label was detected predominantly in the chromosomal area.

L10 ANSWER 18 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

95:333955 The Genuine Article (R) Number: QX432. IMMUNOFLUORESCENT LOCALIZATION OF NUCLEAR-PROTEIN IN POLYTENE CHROMOSOMES OF 2 CHRIONOMID SPECIES - ENDOCHIRONOMUS-TENDENS (FABR) AND GLYPTOTENDIPES-GDRIPEKOVENI KIEFFER (DIPTERA, CHIRONOMIDAE). MICHAILOVA P (Reprint); BATOVA I; KEHAYOV I. BULGARIAN ACAD SCI, INST ZOOL, BU-1000 SOFIA, BULGARIA (Reprint); INST BIOL & IMMUNOL REPROD, BU-1113 SOFIA, BULGARIA. CARYOLOGIA (JUL/DEC 1994) Vol. 47, No. 3-4, pp. 299-310. ISSN: 0008-7114. Pub. country: BULGARIA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A monoclonal **antibody** (Mab **2a8**) has been generated against a DNA tight binding protein of eukaryotic cells. Its distribution was investigated in salivary gland polytene chromosomes of two Chironomid species, Endochironomus tendens and Glyptotendipes gripekoveni, by immunofluorescence. The results indicate: 1. Mab **2a8** is distributed in some distinct condensed bands along the entire lenght of chromosomes; 2. The banding pattern obtained with fluorescent **antibody** does almost strictly correspond to some Hoechst positive bands and to constitutive heterochromatin sites established by ''C'' banding method. Other condensed (Hoechst positive) bands on chromosomes

were Mab **2a8** immunonegative. 3. No immunofluorescent was observed in genetically active regions of polytene chromosomes (puffs, Balbiani rings and nuclear organizer). The mode of distribution in defined bands of polytene chromosomes suggests the residence of this protein in polytene chromosomes, whose presence appears to be well in correlation with the centromere and intercalary heterochromatin regions. This protein exhibits preferential binding to specific chromosome sites containing DNA sequences preferably involved in a specific interaction with target protein. This protein is probably conserved during the evolution being represented in species distant from a phylogenetical point of view (mammalian cells, polytene chromosomes of Chironomid).

L10 ANSWER 19 OF 28 EMBASE
on STN

94232064 EMBASE Document No.: 1994232064. Reactivity of monoclonal **antibodies** to Pseudomonas aeruginosa isolates from hospitalized adults and patients with cystic fibrosis. Torensma R.; Fluit A.C.; Verhoef J.. Division of Hematology, University Hospital Nijmegen, Geert Grooteplein 8,6500 IIB Nijmegen, Netherlands. Clinical Infectious Diseases 19/1 (11-14) 1994.
ISSN: 1058-4838. CODEN: CIDIEL. Pub. Country: United States. Language: English. Summary Language: English.

AB To assess the potential therapeutic use of three human monoclonal **antibodies** (MAbs) and one murine MAb, we tested the reactivity of these MAbs toward 100 clinical isolates of Pseudomonas aeruginosa. Seventy-five isolates were from hospitalized patients, while 25 were recovered from patients with documented cystic fibrosis. Nine isolates showed autoagglutination. The three human MAbs and one murine MAb exhibited agglutination with 81% of the P. aeruginosa isolates obtained from hospitalized patients and with 72% of the isolates from patients with cystic fibrosis. Eight of the autoagglutinating isolates were reactive in whole-cell ELISAs with the MAbs. The isolates recovered from patients with cystic fibrosis were reactive mainly with a MAb that is directed to the outer core of lipopolysaccharide (LPS); they showed hardly any reaction with O antigen-specific MAbs or typing sera, a finding indicating that these isolates lacked the O antigen and that the outer core of the LPS was still present. The reactivity of the MAb specific for the outer core of LPS toward P. aeruginosa isolates from patients with cystic fibrosis has potential value in eradicating P. aeruginosa from these patients.

L10 ANSWER 20 OF 28 MEDLINE on STN DUPLICATE 10

93037260 Document Number: 93037260. PubMed ID: 1416830. Effects of a human antiflagellar monoclonal **antibody** in combination with antibiotics on Pseudomonas aeruginosa infection. Uezumi I; Terashima M; Kohzuki T; Kato M; Irie K; Ochi H; Noguchi H. (Research Laboratories, Sumitomo Pharmaceuticals Co., Ltd., Osaka, Japan.) ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1992 Jun) 36 (6) 1290-5. Journal code: 0315061. ISSN: 0066-4804. Pub. country: United States. Language: English.

AB The in vivo activity of human immunoglobulin M monoclonal **antibody** IN-**2A8**, which is specific for flagellum type b of Pseudomonas aeruginosa, was evaluated in comparison to anti-O antigen (serotype B) MAb KO-2F2 and in combination with antibiotics. IN-**2A8** showed stronger activity than KO-2F2 against subcutaneous infection in burned mice, while it was much less active against intraperitoneal infection in normal mice. In a burn infection model, IN-**2A8** inhibited the increase of bacteria in skin lesions weakly and that in blood significantly, suggesting that it strongly suppressed bacterial spread to blood. The activity of IN-**2A8** in combination with 10 antipseudomonal antibiotics against intraperitoneal infection was examined. Clear additive effect was observed with a combination of either carbapenem or aminoglycoside antibiotics in terms of mouse survival. The administration of an antibiotic, imipenem-cilastatin, simultaneously with or before that of IN-**2A8** gave a combined effect, but the reverse order did not. The combination of IN-**2A8** with

imipenem-cilastatin decreased numbers of viable bacteria in the peritoneal cavity and blood and kept them low for a longer time than did either treatment alone. These results suggest that an antiflagellar monoclonal **antibody** would be effective against systemic infection in combination with some kinds of antibiotics.

L10 ANSWER 21 OF 28 MEDLINE on STN DUPLICATE 11
91100026 Document Number: 91100026. PubMed ID: 1898908. Inhibitory activity on bacterial motility and in vivo protective activity of human monoclonal **antibodies** against flagella of Pseudomonas aeruginosa. Ochi H; Ohtsuka H; Yokota S; Uezumi I; Terashima M; Irie K; Noguchi H. (Laboratory of Biotechnology, Takarazuka Research Center, Sumitomo Chemical Co., Ltd., Hyogo, Japan.) INFECTION AND IMMUNITY, (1991 Feb) 59 (2) 550-4. Journal code: 0246127. ISSN: 0019-9567. Pub. country: United States. Language: English.

AB Three stable hybridoma cell lines, IN-**2A8**, IN-5D6, and ZI-3A8, that secrete human monoclonal **antibodies** (MAbs) specific for b-type flagella of Pseudomonas aeruginosa were established by fusing peripheral blood lymphocytes from healthy volunteers with murine myeloma P3X63-Ag8.653 cells. The immunoglobulin M MAbs reacted specifically with flagellin (Mr, 52,000) by Western blotting (immunoblotting) analysis and bound specifically to clinical isolates belonging to Homma serotypes A, B, H, I, and M at frequencies of 58, 50, 46, 30, and 35%, respectively, but did not bind to any serotype E or G isolates. Overall, the MAbs bound to 31% of the clinical isolates. MAb IN-**2A8** strongly protected burned mice challenged with P. aeruginosa bearing b-type flagella from death following parenteral administration of 0.1 microgram per mouse. This MAb also inhibited P. aeruginosa colony spreading in soft agar at a concentration of more than 1 microgram/ml but only slightly enhanced opsonophagocytosis by human polymorphonuclear leukocytes. A line of evidence suggests that the potent in vivo activity of MAb IN-**2A8** in the burned-mouse model is likely to be caused by its inhibition of bacterial motility after binding to flagella.

L10 ANSWER 22 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
91:69998 The Genuine Article (R) Number: EU973. INHIBITORY ACTIVITY ON BACTERIAL MOTILITY AND INVIVO PROTECTIVE ACTIVITY OF HUMAN MONOCLONAL-**ANTIBODIES** AGAINST FLAGELLA OF PSEUDOMONAS-AERUGINOSA. OCHI H; OHTSUKA H; YOKOTA S; UEZUMI I; TERASHIMA M; IRIE K; NOGUCHI H (Reprint). SUMITOMO CHEM CO LTD, TAKARAZUKA RES CTR, BIOTECHNOL LAB, TAKARAZUKA, HYOGO 665, JAPAN; SUMITOMO PHARMACEUT CO LTD, RES LAB, OSAKA 554, JAPAN. INFECTION AND IMMUNITY (1991) Vol. 59, No. 2, pp. 550-554. Pub. country: JAPAN. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Three stable hybridoma cell lines, IN-**2A8**, IN-5D6, and ZI-3A8, that secrete human monoclonal **antibodies** (MAbs) specific for b-type flagella of Pseudomonas aeruginosa were established by fusing peripheral blood lymphocytes from healthy volunteers with murine myeloma P3X63-Ag8.653 cells. The immunoglobulin M MAbs reacted specifically with flagellin (M(r), 52,000) by Western blotting (immunoblotting) analysis and bound specifically to clinical isolates belonging to Homma serotypes A, B, H, I, and M at frequencies of 58, 50, 46, 30, and 35%, respectively, but did not bind to any serotype E or G isolates. Overall, the MAbs bound to 31% of the clinical isolates. MAb IN-**2A8** strongly protected burned mice challenged with P. aeruginosa bearing b-type flagella from death following parenteral administration of 0.1-mu-g per mouse. This MAb also inhibited P. aeruginosa colony spreading in soft agar at a concentration of more than 1-mu-g/ml but only slightly enhanced opsonophagocytosis by human polymorphonuclear leukocytes. A line of evidence suggests that the potent in vivo activity of MAb IN-**2A8** in the burned-mouse model is likely to be caused by its inhibition of bacterial motility after binding to flagella.

L10 ANSWER 23 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 12
1991:501205 Document No.: PREV199192124165; BA92:124165. IDENTIFICATION AND GENE LOCATION OF TARGET ANTIGENS OF ANTI-HSV MONOCLONAL **ANTIBODIES** . YU Q-G [Reprint author]; ET AL. DEP MICROBIOLOGY, FOURTH MILITARY MED UNIVERSITY, XI' AN. Zhonghua Weishengwuxue He Mianyixue Zazhi, (1991) Vol. 11, No. 4, pp. 212-215.
CODEN: ZWMZDP. ISSN: 0254-5101. Language: CHINESE.
AB From the extracts of herpes simplex virus (HSV) infected BHK-21 cells labelled with [35S]-methionine or [14C]-fructose, one monoclonal **antibody** (McAb), 1D10, precipitated a glycoprotein with a molecular weight of approximately 60 000 daltons, and the other six McAbs, 1A12, Mad-2, 2D11, CM-D3, **2A8** and 1C4, precipitated a group of glycoproteins with molecular weights between 105 000 and 130 000 daltons. Immunoassays of BHK cells infected with HSV-1/HSV-2 intertypic recombinants localized the gene encoding the target antigen of 1D10 to the unique short region (US) at map unit 0.912-0.976 overlapping the gene encoding gD and the genes encoding the target antigens of McAb 1A12, Mad-2, 2D11, CM-D3, **2A8** and 1C4 to the long unique region(UL) between map unit 0.536 and 0.682 overlapping the gene encoding gC. Depending on the reactivity with HSV-1 and HSV-2 infected BHK cells, Mad-2 shows HSV-1 type-specific, CM-D3 shows HSV-2 type-specific and the other McAbs show type-common specific. So Mad-2 is against gC-1, CM-d3 is against gC-2, and 1A12, 2D11, **2A8** and 1C4 are against type-common gC. 1D10 is against type-common gD.

L10 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
1991:40918 Document No. 114:40918 Human monoclonal **antibody** to flagella of Pseudomonas aeruginosa, and its production, characterization, and use. Ochi, Hiroshi; Ohtsuka, Hiroshi; Yokota, Shinichi; Noguchi, Hiroshi; Terashima, Masazumi; Kato, Masuhiro (Sumitomo Chemical Co., Ltd., Japan; Sumitomo Pharmaceuticals Co., Ltd.). Eur. Pat. Appl. EP 383090 A1 19900822, 39 pp. DESIGNATED STATES: R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-101804 19900130. PRIORITY: JP 1989-22245 19890130; JP 1989-271034 19891017.
AB A human monoclonal **antibody** (MAb) specifically binding to flagella of P. aeruginosa is produced by the hybridoma method and has a therapeutic effect on mouse exptl. infection caused by P. aeruginosa at a dose .gtoreq.5 .mu.g/kg body wt. Human B-lymphocytes from peripheral blood of a healthy volunteer having a high **antibody** titer to P. aeruginosa were isolated, suspended in a lymphocyte culturing medium contg. formalin-fixed cells of P. aeruginosa, and cultured for 6 days. The activated lymphocytes were used with mouse myeloma P3x63-Ag8.653 cells and hybridomas producing human MAb to flagellin were selected. MAb IN-**2A8** exerted a definite therapeutic effect at 0.1 and 1 .mu.g/head in mice challenged with P. aeruginosa strains. The LD50 values for challenged mice treated with MAb IN-**2A8** 0.1, IN-**2A8** 0.1 + antibiotic imipenem 100 .mu.g/head, and antibiotic alone were 2.6 .times. 105, 1.1 .times. 106, and 1.7 .times. 105, resp., compared to 1.8 .times. 103 in untreated mice.

L10 ANSWER 25 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
1985:434553 Document No.: PREV198580104545; BA80:104545. THE STUDY OF MONOCLONAL **ANTIBODIES** AGAINST HERPES SIMPLEX VIRUS 3. NEUTRALIZATION IN-VITRO AND PROTECTION IN-VIVO. GAO Q [Reprint author]; JIANG S-Z; MA W-Y; DAI D-S. FOURTH MIL MED COLL, XIAN. Zhonghua Weishengwuxue He Mianyixue Zazhi, (1985) Vol. 5, No. 4, pp. 233-235.
CODEN: ZWMZDP. ISSN: 0254-5101. Language: CHINESE.
AB The neutralization in vitro and protective effect in vivo of five McAb against HSV were studied in (1) tissue cutlure neutralization test, (2) ADCC effect on BHK cells infected by HSV-1, (3) protective effect on rabbit skin infected locally by HSV-1, (4) protective effect on nude mouse lethally infected by HSV-1. The results showed that McAb 2C5 which had a high neutralization titer and ADCC activity protected rabbits and nude mouse from HSV local or lethal infection. McAB 1D10 had no neutralization